```
=> fil wpix

FILE 'WPIX' ENTERED AT 12:47:41 ON 27 MAY 2004
COPYRIGHT (C) 2004 THOMSON DERWENT

FILE LAST UPDATED:          25 MAY 2004      <20040525/UP>
MOST RECENT DERWENT UPDATE:    200433        <200433/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
    http://thomsonderwent.com/coverage/latestupdates/          <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://thomsonderwent.com/support/userguides/              <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
    DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
    FIRST VIEW - FILE WPIFV. FREE CONNECT HOUR UNTIL 1 MAY 2004.
    FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv  <<<

>>> NEW! IMPROVE YOUR LITIGATION CHECKING AND INFRINGEMENT
    MONITORING WITH LITALERT. FIRST ACCESS TO RECORDS OF IP
    LAWSUITS FILED IN THE 94 US DISTRICT COURTS SINCE 1973.
    FOR FURTHER DETAILS:
    http://www.thomsonscientific.com/litalert          <<<

>>> THE DISPLAY LAYOUT HAS BEEN CHANGED TO ACCOMODATE THE
    NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION
    NUMBERS. SEE ALSO:
    http://www.stn-international.de/archive/stnews/news0104.pdf <<<

>>> SINCE THE FILE HAD NOT BEEN UPDATED BETWEEN APRIL 12-16
    THERE WAS NO WEEKLY SDI RUN  <<<

=> d que l100
L95          485 SEA FILE=WPIX ABB=ON  PLU=ON  A61K031-69/IPC
L96         1525 SEA FILE=WPIX ABB=ON  PLU=ON  (B05-B01A OR C05-B01A)/MC
L97         1861 SEA FILE=WPIX ABB=ON  PLU=ON  L95 OR L96
L98         6803 SEA FILE=WPIX ABB=ON  PLU=ON  (B12-M03 OR C12-M03)/MC
L99           14 SEA FILE=WPIX ABB=ON  PLU=ON  L97 AND L98
L100           1 SEA FILE=WPIX ABB=ON  PLU=ON  L99 AND MICROEMULSION/TI,TT


=> d l100 iall abeq tech abex

L100 ANSWER 1 OF 1  WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER:     1993-351328 [44]   WPIX
DOC. NO. CPI:         C1993-155866
TITLE:                Therapeutic or diagnostic compsn. targets specific cells
                      - by using specific ligand associated with
                      lipoprotein(s), microemulsion particles,
                      lipsome(s) or micelles containing the active component.
DERWENT CLASS:        B01 B04 B07 C03 C07
INVENTOR(S):          KINNUNEN, P K J
PATENT ASSIGNEE(S):   (KINN-I) KINNUNEN P K J
```

COUNTRY COUNT: 43
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9320800	A1	19931028	(199344)*	EN	19	A61K009-127
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE						
W: AT AU BB BG BR CA CH CZ DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US VN						
AU 9338925	A	19931118	(199410)			A61K009-127
EP 634926	A1	19950125	(199508)	EN		A61K009-127
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE						
JP 07505408	W	19950615	(199532)			A61K009-107

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9320800	A1	WO 1993-FI149	19930407
AU 9338925	A	AU 1993-38925	19930407
EP 634926	A1	EP 1993-907890	19930407
		WO 1993-FI149	19930407
JP 07505408	W	JP 1993-518017	19930407
		WO 1993-FI149	19930407

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9338925	A	Based on	WO 9320800
EP 634926	A1	Based on	WO 9320800
JP 07505408	W	Based on	WO 9320800

PRIORITY APPLN. INFO: US 1992-865256 19920408
REFERENCE PATENTS: WO 8607540
INT. PATENT CLASSIF.:
MAIN: A61K009-107; A61K009-127
SECONDARY: A61K047-48; A61K049-04
BASIC ABSTRACT:

WO 9320800 A UPAB: 19931213
A compsn. for theraputic or diagnostic use comprises a carrier and a lysosmotropic agent. The carrier consists of lipoproteins, other types of microemulsion particles. liposomes and micelles containing a lipo- or amphi-philic active agent, associated with at least one ligand which is complementary to and recognisable by a specific cell receptor.

The carrier is pref. reconstituted Low Densith Lipoprotein (LDL) and the lysosomotropic agent is pref. Triton WR 1339 ethyl oleate. The theraputic or diagnostic agent is pref. a light sensitiser (e.g. hematoporphyrin), radiosensitiser (e.g. boronated fatty acid esters), X-ray contrast agent or anti-cancer drug (e.g. doxorubicin, daunomycin or 1-hexadecyl-2-methyl-3-phosphocholine).

Pref. compsn. contains the anti-cancer drug chlorambucil cholesteryl ester. Pref. compsn. comprises a reconstituted LDL containing chlorambucil cholesteryl ester and Triton WR 1339 ethyl oleate.

USE - The compsn. is useful for theraputic and diagnostic treatment of humans and animals. The cell-specific ligand targets the active agent to the site of interest, such as cancerous tissue and therefore concentrates the action at the site. The compsn. is pref. used parenterally.

Dwg.0/2

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B01-D02; C01-D02; B02-D; C02-D; B04-B01B; C04-B01B; B04-C03D; C04-C03D; **B05-B01A**; **C05-B01A**; B05-B01P; C05-B01P; B06-D18; C06-D18; **B12-M03**; **C12-M03**; B12-M11F; C12-M11F

=> FIL STNGUIDE

=>

=> fil zcaplus

FILE 'ZCAPLUS' ENTERED AT 12:40:49 ON 27 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 May 2004 VOL 140 ISS 22
FILE LAST UPDATED: 26 May 2004 (20040526/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 12:40:52 ON 27 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 May 2004 VOL 140 ISS 22
FILE LAST UPDATED: 26 May 2004 (20040526/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil biosis

FILE 'BIOSIS' ENTERED AT 12:40:55 ON 27 MAY 2004

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 May 2004 (20040526/ED)

FILE RELOADED: 19 October 2003.

=> fil uspatfull

FILE 'USPATFULL' ENTERED AT 12:41:00 ON 27 MAY 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 27 May 2004 (20040527/PD)
FILE LAST UPDATED: 27 May 2004 (20040527/ED)
HIGHEST GRANTED PATENT NUMBER: US6742188
HIGHEST APPLICATION PUBLICATION NUMBER: US2004103464
CA INDEXING IS CURRENT THROUGH 27 May 2004 (20040527/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 27 May 2004 (20040527/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2004

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> FIL STNGUIDE

FILE 'STNGUIDE' ENTERED AT 12:41:03 ON 27 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 21, 2004 (20040521/UP).

=> d que l119
L1 (120) SEA FILE=REGISTRY ABB=ON PLU=ON B>=1 AND (4432.3.5)/RID
L2 (5) SEA FILE=HCAPLUS ABB=ON PLU=ON 328563-79-7?
L3 (2) SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND BCH
L4 (1) SEA FILE=HCAPLUS ABB=ON PLU=ON 427880-16-8?
L5 (1) SEA FILE=HCAPLUS ABB=ON PLU=ON 427880-18-0?
L6 (59) SEA FILE=HCAPLUS ABB=ON PLU=ON L1
L7 59 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5
OR L6)
L8 1 SEA FILE=REGISTRY ABB=ON PLU=ON TRIOLEIN/CN

```
L9       111711 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (?GLYCERID? OR ?MONOGLYCERID?
                OR ?DIGLYCERID? OR ?TRIGLYCERID? OR ?TRIOLEIN?)/CW
L10       14129 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MONOGLYCERIDES+PFT,NT,RT/CT
L11       13112 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIGLYCERIDES+PFT,NT,RT/CT
L12      127444 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLYCERIDES+PFT,NT,RT/CT
L13        3757 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8
L14           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND (L9 OR L10 OR L11 OR
                L12 OR L13)
L15           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (?GLYCER? OR ?TRIOLEIN?) AND
                L7
L16           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  LYSOZYME/CN
L18          43 SEA FILE=REGISTRY ABB=ON  PLU=ON  AVIDIN/CNS
L19           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  POLYLYSINE/CN
L20       24723 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR L18 OR L19
L21        4016 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (?LYSOZYM? OR ?AVIDIN? OR
                ?POLYLYS?)/CW
L22       46237 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?LYSOZYM? OR ?AVIDIN? OR
                ?POLYLYS?
L23       28338 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LYSOZYME/CT OR AVIDINS/CT OR
                (POLYLYSINE/CT OR POLY-L-LYSINE/CT OR "POLY-L-LYSINE, SRU"/CT)
L24           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L20 OR L21 OR L22 OR L23)
                AND L7
L25       67910 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (?LIPOPROTEIN? OR ?CHYLOMICRON
                ?)/CW
L26       92431 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LIPOPROTEINS+PFT,NT,RT/CT
L27       42248 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CHYLOMICRONS/CT OR CHYLOMICRON
                /CT OR "FATS AND GLYCERIDIC OILS"/CT
L28           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L25 OR L26 OR L27) AND L7
L29           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (LDL? OR ?VLDL? OR IDL? OR
                HDL? OR ?CHYLOMICRON?) AND L7
L30 (       120)SEA FILE=REGISTRY ABB=ON  PLU=ON  B>=1 AND (4432.3.5)/RID
L31 (         5)SEA FILE=HCAPLUS ABB=ON  PLU=ON  328563-79-7?
L32 (         2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 AND BCH
L33 (         1)SEA FILE=HCAPLUS ABB=ON  PLU=ON  427880-16-8?
L34 (         1)SEA FILE=HCAPLUS ABB=ON  PLU=ON  427880-18-0?
L35 (        59)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30
L36 (        59)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 OR (L33 OR L34 OR L35)
L37 (     97751)SEA FILE=HCAPLUS ABB=ON  PLU=ON  (?SPHINGOMYELIN? OR ?CEPHALIN?
                 OR ?PHOSPHATIDYL? OR ?PHOSPHATIDIC? OR ?ISOLECTIN? OR
                ?PHOSPHOLIPID?)/CW
L38 (         3)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L37
L39 (        73)SEA FILE=HCAPLUS ABB=ON  PLU=ON  57-88-5? (L) (?BORO? OR
                ?BORAN? OR ?BORAX? OR ?BORAH? OR ?BORIC?)
L40 (       474)SEA FILE=HCAPLUS ABB=ON  PLU=ON  57-88-5? (L) (?EMULSION?)
L41 (         2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 AND (?BORO? OR ?BORAN? OR
                ?BORAX? OR ?BORAH? OR ?BORIC?)
L42 (        75)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L39 OR L41
L43 (        11)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L42 AND L37
L44          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 OR L43
L45 (       120)SEA FILE=REGISTRY ABB=ON  PLU=ON  B>=1 AND (4432.3.5)/RID
L46 (         5)SEA FILE=HCAPLUS ABB=ON  PLU=ON  328563-79-7?
L47 (         2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L46 AND BCH
L48 (         1)SEA FILE=HCAPLUS ABB=ON  PLU=ON  427880-16-8?
L49 (         1)SEA FILE=HCAPLUS ABB=ON  PLU=ON  427880-18-0?
L50 (        59)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45
L51 (     97751)SEA FILE=HCAPLUS ABB=ON  PLU=ON  (?SPHINGOMYELIN? OR ?CEPHALIN?
                 OR ?PHOSPHATIDYL? OR ?PHOSPHATIDIC? OR ?ISOLECTIN? OR
                ?PHOSPHOLIPID?)/CW
L52 (        73)SEA FILE=HCAPLUS ABB=ON  PLU=ON  57-88-5? (L) (?BORO? OR
                ?BORAN? OR ?BORAX? OR ?BORAH? OR ?BORIC?)
```

L53 (474) SEA FILE=HCAPLUS ABB=ON PLU=ON 57-88-5? (L) (?EMULSION?)
L54 (2) SEA FILE=HCAPLUS ABB=ON PLU=ON L53 AND (?BORO? OR ?BORAN? OR ?BORAX? OR ?BORAH? OR ?BORIC?)
L55 (75) SEA FILE=HCAPLUS ABB=ON PLU=ON L52 OR L54
L56 (168532) SEA FILE=HCAPLUS ABB=ON PLU=ON (PHOSPHOLIPIDS/CT OR "ALPHA LIPID 300"/CT OR ASOLECTINS/CT OR AZOLECTINS/CT OR DARMSTOFF/CT OR "EMULPUR N"/CT OR "EPIKURON 110"/CT OR "EPUIKURON 170"/CT OR "LIPOID E 80"/CT OR "NAT 3003"/CT OR "NAT 89"/CT OR "OVOTHIN 120"/CT OR "OVOTHIN 170"/CT OR PHOSPHODERM/CT OR PHOSPHOLIPINS/CT OR PLATELIN/CT OR GLYCEROPHOSPHOLIPIDS/CT OR CEPHALINS/CT OR DIPHOSPHOINOSITIDES/CT OR LECITHIN/CT OR LYSOPHOSPHOLIPIDS/CT OR LYSOPHOSPHATIDALETHANOLAMINES/CT OR LYSOPHOSPHATIDALINOSITOLS/CT OR LYSOPHOSPHATIDES/CT OR LYSOCARDIOLIPINS/CT OR LYSOCEPHALINS/CT OR LYSOCYTHINS/CT OR LYSOLECITHIN/CT OR LYSOLECITHINS/CT OR LYSOPHOSPHATIDALCHOLINES/CT OR LYSOPHOSPHATIDALINOSITOLS/CT OR LYSOPHOSPHATIDALSERINES/CT OR LYSOPHOSPHATIDALTHREONINES/CT OR "LYSOPHOSPHATIDIC ACID"/CT OR "LYSOPHOSPHATIDIC ACIDS"/CT OR LYSOPHOSPHATIDYLCHOLINES/CT OR LYSOPHOSPHATIDYLETHANOLAMINE/CT OR LYSOPHOSPHATIDYLETHANOLAMINES/CT OR LYSOPHOSPHATIDYLGLYCEROLS/CT OR LYSOPHOSPHATIDYLINOSITOLS/CT OR LYSOPHOSPHATIDYLSERINES/CT OR LYSOPHOSPHATIDYLTHREONINES/CT OR LYSOPHOSPHOINOSITIDES/CT OR LYSOPLASMALOGENS/CT OR "PHOSPHATIDES (L) ALKALOIDAL, PYRROLOPHENANTHRIDINE"/CT OR "PHOSPHATIDES (L) PHOSPHATIDYLBUTANOLS"/CT OR "PHOSPHATIDES (L) PHOSPHATIDYLETHANOLS"/CT OR "PHOSPHATIDIC ACIDS"/CT OR "DIPALMITOYLPHOSPHATIDIC ACID"/CT OR "LYSOPHOSPHATIDIC ACID"/CT OR "LYSOPHOSPHATIDIC ACIDS"/CT OR "PLASMALOGENIC ACIDS"/CT OR PHOSPHATIDYLCHOLINES/CT OR 1-PALMITOYL-2-OLEOYL-L-A-PHOSPHATIDYLCHOLINE/CT OR 1-PALMITOYL-2-OLEOYLPHOSPHATIDYLCHOLINE/CT OR DILAUROYLPHOSPHATIDYLCHOLINE/CT OR DIMYRISTOYLPHOSPHATIDYLCHOLINE/CT OR DIOLEOYLPHOSPHATIDYLCHOLINE/CT OR DIPALMITOYLPHOSPHATIDYLCHOLINE/CT OR DISTEAROYLPHOSPHATIDYLCHOLINE/CT OR GLYCEROPHOSPHOCHOLINE/CT OR GLYCOLLECITHINS/CT OR L-DIMYRISTOYLPHOSPHATIDYLCHOLINE/CT OR L-DIOLEOYLPHOSPHATIDYLCHOLINE/CT OR L-DIPALMITOYLPHOSPHATIDYLCHOLINE/CT OR L-DISTEAROYLPHOSPHATIDYLCHOLINE/CT OR LYSOCYTHINS/CT OR LYSOLECITHIN/CT OR LYSOLECITHINS/CT OR LYSOPHOSPHATIDYLCHOLINES/CT OR "PLATEL
L57 (59) SEA FILE=HCAPLUS ABB=ON PLU=ON (L45 OR L46 OR L47 OR L48 OR L49 OR L50)
L58 33 SEA FILE=HCAPLUS ABB=ON PLU=ON (L57 OR L55) AND (L51 OR L56)
L59 35 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 OR L15 OR L24 OR L28 OR L29 OR L44 OR L58
L60 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND ?LIPID?
L61 17 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND (?LIPID? OR ?LIPO?)
L62 43 SEA FILE=HCAPLUS ABB=ON PLU=ON (L59 OR L60 OR L61)
L65 30 SEA FILE=HCAPLUS ABB=ON PLU=ON L62 AND (PRY<2002 OR PY<2002 OR AY<2002)
L73 2449541 SEA FILE=HCAPLUS ABB=ON PLU=ON (?COLLOID? OR ?EMULS? OR ?LAYER? OR ?CORE? OR ?AMPHIPATH? OR ?HYDROPHOB? OR ?HYDROPHIL? OR ?LAMELL? OR ?MICELL?)
L74 18 SEA FILE=HCAPLUS ABB=ON PLU=ON L65 AND L73
L75 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L74 NOT ((FOOD OR FEED CHEMISTRY)/SC OR (FOSSIL FUELS)/SC OR (CARBOHYDRATES)/SC)
L76 351453 SEA FILE=HCAPLUS ABB=ON PLU=ON (DRUG DELIVER? OR RADIOTHER? OR IMAG? OR PHARMACEUT? OR DIAGNOS?)/CW
L77 17 SEA FILE=HCAPLUS ABB=ON PLU=ON L76 AND L65
L78 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L77 NOT L74
L79 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L78 NOT ((BIOCHEMICAL GENETICS)/SC OR SAIMIRI/IT)

```
L80           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 NOT (L74 OR L78)
L81           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L80 AND CARBOHYDRATES/SC
L82          20 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 OR L75 OR L81
L119         16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L82 NOT (MONOSACCHARIDE OR
                SPIN LABELS OR REDUCING SUGARS OR CORNEUM)/TI


=> d que l120
L83         168 SEA FILE=BIOSIS ABB=ON  PLU=ON  ?CHOLEST? (L) (?BORO? OR
                ?BORIC? OR ?BORAN? OR ?BORAX?)
L84      633075 SEA FILE=BIOSIS ABB=ON  PLU=ON  (?COLLOID? OR ?EMULS? OR
                ?LAYER? OR ?CORE? OR ?AMPHIPATH? OR ?HYDROPHOB? OR ?HYDROPHIL?
                OR ?LAMEL? OR ?MICELL?)
L86          28 SEA FILE=BIOSIS ABB=ON  PLU=ON  L84 AND L83
L87          10 SEA FILE=BIOSIS ABB=ON  PLU=ON  L86 AND (TETRAPHENYLBORON OR
                BORON NEUTRON-CAPTURE OR BORON NEUTRON CAPTURE OR MURINE
                TUMORS OR XENOGRAFTS OR BNCT OR VLDL OR CHOLESTERYL CARBORANE)/
                TI
L88          31 SEA FILE=BIOSIS ABB=ON  PLU=ON  L83 AND (?DRUG? OR ?RADIOTHER?
                OR ?IMAG? OR ?PHARMACEUT?)
L89          25 SEA FILE=BIOSIS ABB=ON  PLU=ON  L88 NOT L86
L90           6 SEA FILE=BIOSIS ABB=ON  PLU=ON  L89 AND (BRATTLEBORO OR DRUG
                DELIVERY OR BORON NEUTRON CAPTURE)/TI
L91           5 SEA FILE=BIOSIS ABB=ON  PLU=ON  L90 NOT CORTICAL/TI
L93          15 SEA FILE=BIOSIS ABB=ON  PLU=ON  L87 OR L91
L120         13 SEA FILE=BIOSIS ABB=ON  PLU=ON  L93 NOT (BRATTLEBORO OR
                TETRAPHENYLBORON)/TI


=> d que l114
L68         120 SEA FILE=REGISTRY ABB=ON  PLU=ON  B>=1 AND (4432.3.5)/RID
L70           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L68 AND USPATFULL/LC
L72           4 SEA FILE=USPATFULL ABB=ON  PLU=ON  L70
L101          2 SEA FILE=USPATFULL ABB=ON  PLU=ON  L72 AND (A61K049-00 OR
                C07J009-00)/ICM
L114          2 SEA FILE=USPATFULL ABB=ON  PLU=ON  L101 AND (?EMULS? OR
                ?LAYER? OR ?LAMELL? OR ?MICELL? OR ?AMPHIPATH? OR ?COLLOID? OR
                ?HYDROPHOB? OR ?HYDROPHIL?)/BI


=> dup rem l119 l120 l114

FILE 'HCAPLUS' ENTERED AT 12:41:44 ON 27 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 12:41:44 ON 27 MAY 2004
COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'USPATFULL' ENTERED AT 12:41:44 ON 27 MAY 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
PROCESSING COMPLETED FOR L119
PROCESSING COMPLETED FOR L120
PROCESSING COMPLETED FOR L114
L131         26 DUP REM L119 L120 L114 (5 DUPLICATES REMOVED)
                ANSWERS '1-16' FROM FILE HCAPLUS
                ANSWERS '17-25' FROM FILE BIOSIS
                ANSWER '26' FROM FILE USPATFULL
```

=> FIL STNGUIDE

FILE 'STNGUIDE' ENTERED AT 12:42:52 ON 27 MAY 2004

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 21, 2004 (20040521/UP).

=> d l131 iall hitstr
YOU HAVE REQUESTED DATA FROM FILE 'USPATFULL, HCAPLUS, BIOSIS' - CONTINUE? (Y)/N:y

L131 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 1999:602799 HCAPLUS
DOCUMENT NUMBER: 131:337242
ENTRY DATE: Entered STN: 23 Sep 1999
TITLE: Synthesis of boron-containing cholesterol derivatives for incorporation into **unilamellar liposomes** and evaluation as potential agents for BNCT
AUTHOR(S): Feakes, Debra A.; Spinler, Jennifer K.; Harris, Fred R.
CORPORATE SOURCE: Chemistry Department, Southwest Texas State University, San Marcos, TX, 78666, USA
SOURCE: Tetrahedron (**1999**), 55(37), 11177-11186
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 32-7 (Steroids)
Section cross-reference(s): 29

ABSTRACT:
Four carborane-containing derivs. of cholesterol were prepared for incorporation into the **bilayer** of **unilamellar liposomes** and evaluation as potential agents for boron neutron capture therapy. The derivs. enable the evaluation of the linker moiety and the type of carborane head group on the **bilayer** stability and ultimate in vivo tumor specificity.

SUPPL. TERM: cholesterol boron contg deriv prepn; BNCT boron contg cholesterol
INDEX TERM: Radiotherapy
(boron-neutron capture; synthesis of boron-containing cholesterol derivs. for incorporation into **unilamellar liposomes** and evaluation as potential agents for BNCT)
INDEX TERM: Carboranes
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of boron-containing cholesterol derivs.)
INDEX TERM: 57-88-5, Cholesterol, reactions 17702-41-9, Decaborane 20739-58-6, 2-Octyn-1-ol
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of boron-containing cholesterol derivs.)
INDEX TERM: 871-91-0P, 7-Octyn-1-ol 13860-68-9P 245436-38-8P **249903-49-9P 249903-50-2P** 249903-52-4P 249903-53-5P, 1,2-Dicarbadodecaborane(12)-1-hexanol

249903-54-6P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of boron-containing cholesterol derivs.)

INDEX TERM: **250220-21-4P 250220-23-6P**
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of boron-containing cholesterol derivs.)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

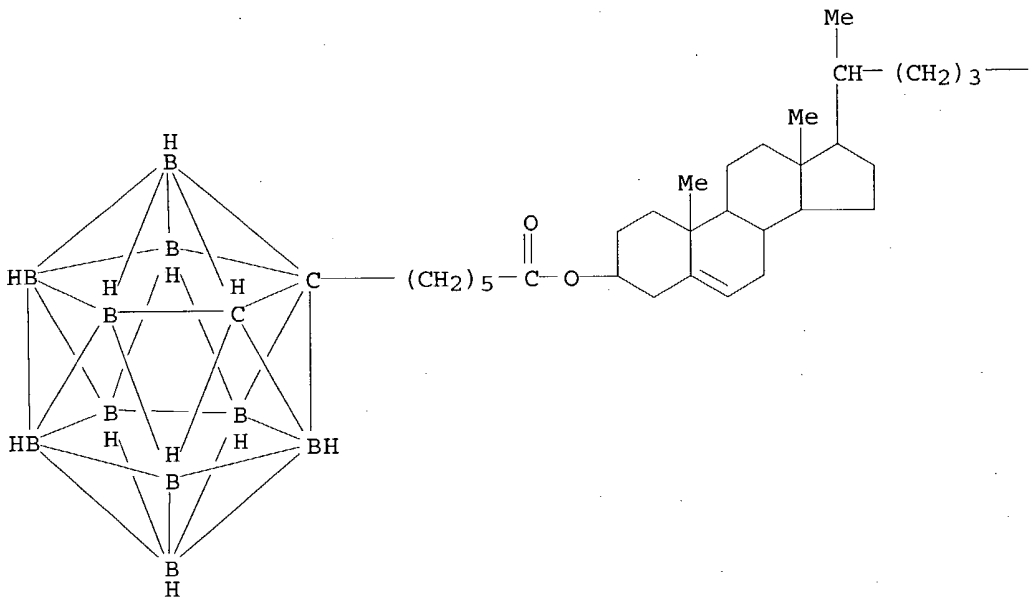
(1) Clendonen, N; Neurosurgery 1990, V26, P47
(2) Coderre, J; Cancer Res 1988, V48, P6313 HCAPLUS
(3) Deamer, D; Lipsomes 1983, P31
(4) Fairchild, R; J Radiat Oncol Biol Phys 1985, V11, P831 HCAPLUS
(5) Feakes, D; Proc Natl Acad Sci USA 1994, V91, P3029 HCAPLUS
(6) Feakes, D; Proc Natl Acad Sci USA 1995, V92, P1367 HCAPLUS
(7) Fraley, R; Biochemistry 1981, V20, P6978 HCAPLUS
(8) Gabel, D; Cancer Res 1987, V47, P5451 HCAPLUS
(9) Hawthorne, M; Inorg Synth 1967, V9, P16 HCAPLUS
(10) Hawthorne, M; Inorg Synth 1967, V10, P91 HCAPLUS
(11) Macaulay, S; J Org Chem 1980, V45, P734 HCAPLUS
(12) Proffitt, R; J Nucl Med 1983, V24, P45 HCAPLUS
(13) Shelly, K; Proc Natl Acad Sci USA 1992, V89, P9039 HCAPLUS
(14) Slatkin, D; Biochem Pharmacol 1986, V35, P1771 HCAPLUS
(15) Soloway, A; Medicinal Chem 1967, V10, P714 HCAPLUS
(16) Srivastava, R; J Org Chem 1997, V62, P8730 HCAPLUS
(17) Straubinger, R; Biochemistry 1990, V29, P4929 HCAPLUS
(18) Straubinger, R; Cell 1983, V32, P1069 HCAPLUS
(19) Sweet, W; Pharmacol Exp Ther 1962, V137, P263 HCAPLUS
(20) Tomita, H; Inorg Chem 1991, V30, P812 HCAPLUS
(21) Wallingford, R; J Nucl Med 1985, V26, P1180 HCAPLUS

IT **249903-49-9P 249903-50-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of boron-containing cholesterol derivs.)

RN 249903-49-9 HCAPLUS

CN Cholest-5-en-3-ol (3β)-, 6-(1,2-dicarbadodecaboran(12)-1-yl)hexanoate (9CI) (CA INDEX NAME)

PAGE 1-A

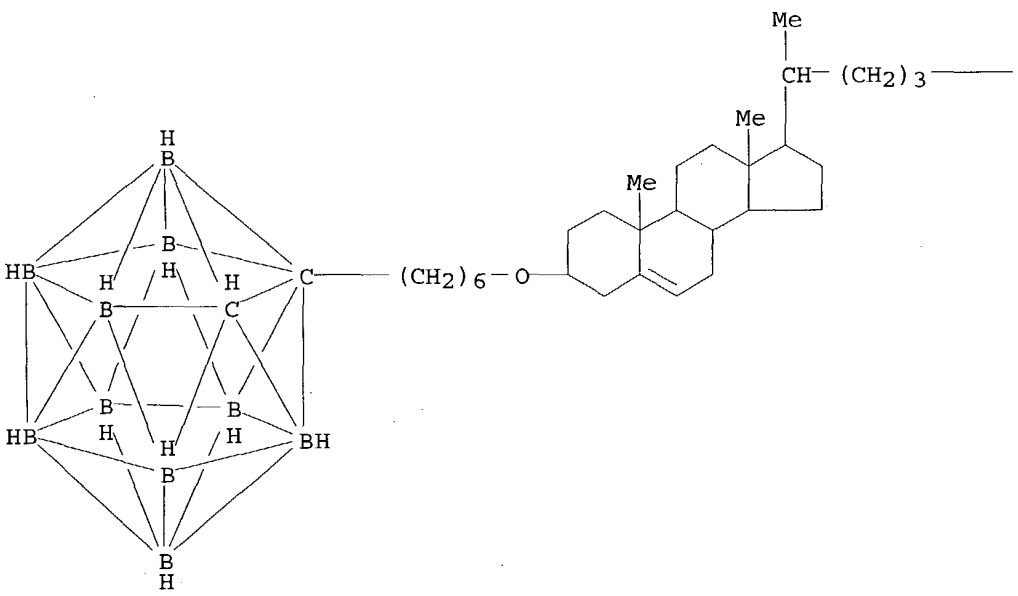


PAGE 1-B

— $CHMe_2$

RN 249903-50-2 HCAPLUS
CN 1,2-Dicarbadodecaborane(12), 1-[6-[(3β)-cholest-5-en-3-yloxy]hexyl]-
(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

— $CHMe_2$

IT **250220-21-4P 250220-23-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of boron-containing cholesterol derivs.)
RN 250220-21-4 HCAPLUS
CN 1-Butanaminium, N,N,N-tributyl-, 7-[6-[(3β)-cholest-5-en-3-yloxy]-6-oxohexyl]undecahydro-7,8-dicarbaundecaborate(1-) (9CI) (CA INDEX NAME)

CM 1

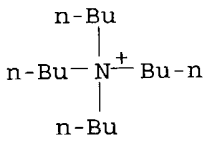
CRN 250220-20-3
CMF C35 H66 B9 O2
CCI CCS

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

CM 2

CRN 10549-76-5
CMF C16 H36 N

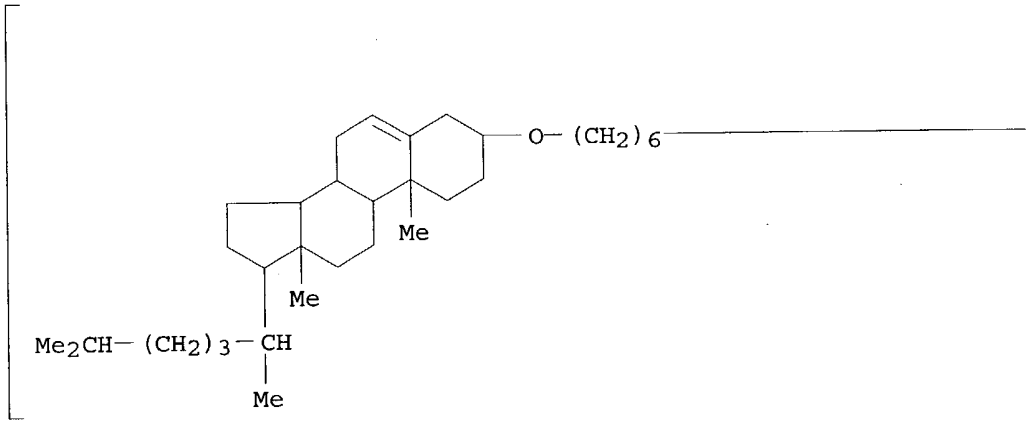


RN 250220-23-6 HCAPLUS
CN 1-Butanaminium, N,N,N-tributyl-, 7-[6-[(3β)-cholest-5-en-3-yloxy]hexyl]undecahydro-7,8-dicarbaundecaborate(1-) (9CI) (CA INDEX NAME)

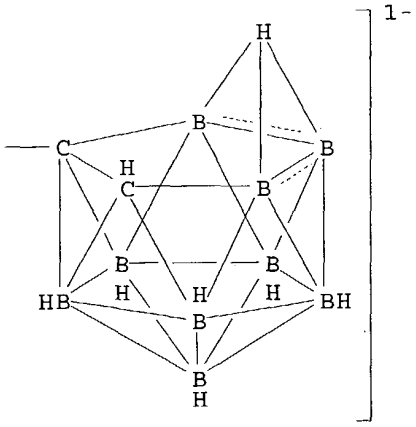
CM 1

CRN 250220-22-5
CMF C35 H68 B9 O
CCI CCS

PAGE 1-A

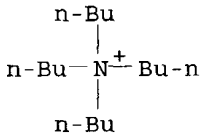


PAGE 1-B



CM 2

CRN 10549-76-5
CMF C16 H36 N



=> d l131 iall hitstr 2-16
YOU HAVE REQUESTED DATA FROM FILE 'USPATFULL, HCAPLUS, BIOSIS' - CONTINUE? (Y)/N:y

L131 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1998:173232 HCAPLUS
DOCUMENT NUMBER: 128:267754
ENTRY DATE: Entered STN: 25 Mar 1998
TITLE: Model studies directed toward the application of boron neutron capture therapy to rheumatoid arthritis: boron delivery by liposomes in rat collagen-induced arthritis
AUTHOR(S): Watson-Clark, Rachel A.; Banquerigo, Mona Lisa; Shelly, Kenneth; Hawthorne, M. Frederick; Brahn, Ernest
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of California, Los Angeles, CA, 90095, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1998**), 95(5), 2531-2534
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal

LANGUAGE: English
CLASSIFICATION: 8-9 (Radiation Biochemistry)
Section cross-reference(s): 63

ABSTRACT:
The application of boron neutron capture therapy to rheumatoid arthritis requires the selective delivery df the boron-10 isotope to the synovitis tissue. The use of liposomes as a boron delivery method has been explored through the measurement of the time course biodistribution of boron in rats with collagen-induced arthritis (CIA). Small **unilamellar** vesicles were composed of a 1:1 mixture of distearoylphosphatidylcholine and cholesterol, incorporated K[nido-7-CH3(CH2)15-7,8-C2B9H11] as an addend in the lipid ***bilayer*** and encapsulated Na3[α2-B20H17NH2CH2CH2NH2] in the aqueous ***core.*** The tissue concentration of boron delivered by liposomes was determined by
inductively coupled plasma-atomic emission spectroscopy after i.v. injection of liposome suspensions into Louvain rats with CIA. With the low injected doses of boron used [13-18 mg of boron per kg (body weight)], the peak boron concentration observed in arthritic synovium was 29 μg of boron per g of tissue. The highest synovium/blood boron ratio observed was 3.0, when the synovial boron concentration was 22
μg of boron per g of tissue. In an attempt to increase the synovium/blood boron ratio by lowering the blood boron concentration, a liposomal formulation characterized by a shorter blood clearance time was examined Thus, the biodistribution of liposomes with addnl. K[nido-7-CH3(CH2)15-7,8-C2B9H11] incorporated in the vesicle membrane not only demonstrated more rapid blood clearance and slightly higher synovium/blood boron ratios but also exhibited reduced boron uptake in synovial tissue. These studies with boron neutron capture therapy for CIA suggest that this form of therapy may be feasible in the treatment of rheumatoid arthritis.

SUPPL. TERM: boron neutron capture therapy rheumatoid arthritis; liposomal boron delivery synovial tissue

INDEX TERM: Radiotherapy
(boron-neutron capture; model studies directed toward application of boron neutron capture therapy to rheumatoid arthritis: boron delivery by liposomes in collagen-induced arthritis)

INDEX TERM: Drug delivery systems
(liposomes; model studies directed toward application of boron neutron capture therapy to rheumatoid arthritis: boron delivery by liposomes in collagen-induced arthritis)

INDEX TERM: Rheumatoid arthritis
Synovial membrane
(model studies directed toward application of boron neutron capture therapy to rheumatoid arthritis: boron delivery by liposomes in collagen-induced arthritis)

INDEX TERM: 165290-42-6 180907-06-6
ROLE: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(model studies directed toward application of boron neutron capture therapy to rheumatoid arthritis: boron delivery by liposomes in collagen-induced arthritis)

INDEX TERM: **57-88-5**, Cholesterol, uses **4539-70-2**, Distearoylphosphatidylcholine
ROLE: MOA (Modifier or additive use); USES (Uses)
(model studies directed toward application of **boron** neutron capture therapy to rheumatoid arthritis: **boron** delivery by liposomes in

collagen-induced arthritis)

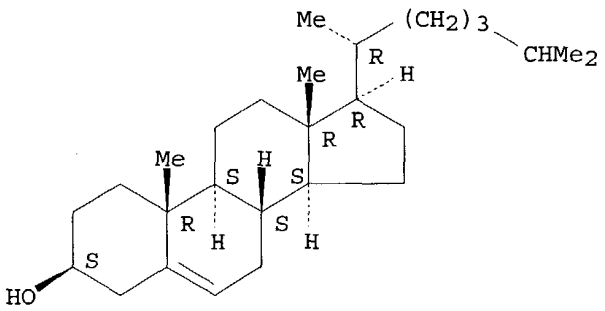
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Binello, E; Advances in Neutron Capture Therapy 1997, VI, P459
(2) Fairchild, R; J Radiat Oncol Biol Phys 1985, V11, P831 HCAPLUS
(3) Feakes, D; Proc Natl Acad Sci USA 1994, V91, P3029 HCAPLUS
(4) Feakes, D; Proc Natl Acad Sci USA 1995, V92, P1367 HCAPLUS
(5) Georgiev, E; Inorg Chem 1996, V35, P5412 HCAPLUS
(6) Harling, O; Nucl Sci Eng 1992, V110, P330 HCAPLUS
(7) Harris, E; Rheumatoid Arthritis 1997, Pxix
(8) Hwang, K; Liposomes:From Biophysics to Therapeutics 1987, P109
(9) Johnson, D; Anal Chim Acta 1992, V270, P223 HCAPLUS
(10) Johnson, L; Cancer Neutron Capture Therapy 1996, P183 HCAPLUS
(11) Kelley, W; Textbook of Rheumatology 1989, P1934
(12) Locher, G; Am J Roentogenol Radium Ther 1936, V36, P1 HCAPLUS
(13) Peacock, D; Cell Immun 1995, V160, P178 HCAPLUS
(14) Peacock, D; J Exp Med 1992, V175, P1135 HCAPLUS
(15) Shelly, K; Proc Natl Acad Sci USA 1992, V89, P9039 HCAPLUS
(16) Straubinger, R; Biochemistry 1990, V29, P4929 HCAPLUS

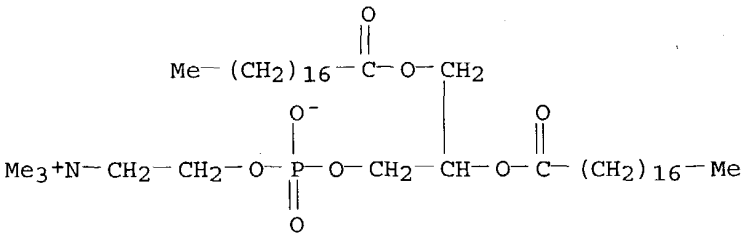
IT **57-88-5**, Cholesterol, uses **4539-70-2**, Distearoylphosphatidylcholine
RL: MOA (Modifier or additive use); USES (Uses)
(model studies directed toward application of **boron** neutron capture therapy to rheumatoid arthritis: **boron** delivery by liposomes in collagen-induced arthritis)

RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



L131 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1998:399473 HCAPLUS
DOCUMENT NUMBER: 129:99958
ENTRY DATE: Entered STN: 01 Jul 1998
TITLE: Liposomes containing boronophenylalanine for boron neutron capture therapy
AUTHOR(S): Perugini, P.; Pavanetto, F.
CORPORATE SOURCE: Dep. of Pharmaceutical Chem., Univ. of Pavia, Pavia, 27100, Italy
SOURCE: Journal of Microencapsulation (1998), 15(4), 473-483
CODEN: JOMIEF; ISSN: 0265-2048
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 63-6 (Pharmaceuticals)
Section cross-reference(s): 8

ABSTRACT:
In the present work, liposomes loaded with boronophenylalanine (BPA), with or without stabilization, were formulated for the application in boron neutron capture therapy. BPA was encapsulated into liposomes as a complex with fructose, but also as a free drug in 2 different pH buffers. The influence of critical variables (cholesterol content, drug:lipid molar ratio, osmotic stress of liposomes containing hyperosmotic drug solution) on liposome morphol. and drug content
was evaluated. The drug content and dissoln. profile of different BPA loaded liposomes were also studied. The phys. stability of liposomes in terms of changes in the size distribution in different osmotic pressure buffers and the chemical oxidation of phospholipids during storing conditions were investigated. The
encapsulation efficiencies of all formulations were always satisfactory, being between 20-48%; even when the liposomes were exposed to high osmotic stress, the particle size was below 200 nm. The BPA-fructose complex loaded liposomes showed a slower drug release profile.

SUPPL. TERM: liposomes boronophenylalanine boron neutron capture therapy
INDEX TERM: Radiotherapy
(boron-neutron capture; liposomes containing boronophenylalanine for boron neutron capture therapy)
INDEX TERM: **Lecithins**
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(egg yolk; liposomes containing boronophenylalanine for boron neutron capture therapy)
INDEX TERM: Dissolution rate
Encapsulation
Particle size distribution

(liposomes containing boronophenylalanine for boron neutron capture therapy)

INDEX TERM: Drug delivery systems
(liposomes, **unilamellar**; liposomes containing boronophenylalanine for boron neutron capture therapy)

INDEX TERM: **Gangliosides**
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monosialogangliosides; liposomes containing boronophenylalanine for boron neutron capture therapy)

INDEX TERM: 57-48-7, Fructose, biological studies **57-88-5**, Cholesterol, biological studies 90580-64-6, DL-p-Boronophenylalanine
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing **boronophenylalanine** for **boron** neutron capture therapy)

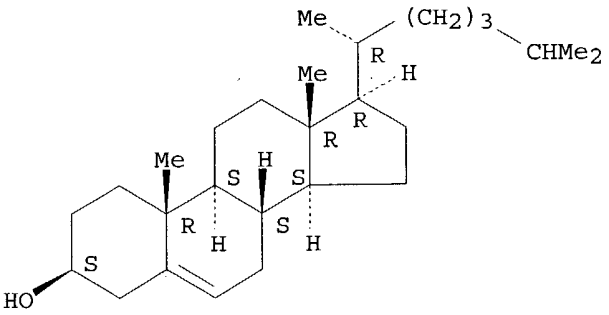
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

(1) Barth, R; Cancer 1992, V70, P2995 MEDLINE
(2) Gabizon, A; Proceedings of the National Academy of Science USA 1988, V85, P6949 HCAPLUS
(3) Hawthorne, M; Angewandte Chemie International Edition in English 1993, V32, P950
(4) Mallesch, J; International Journal of Radiation Oncology, Biology and Physics 1994, V28, P1183 MEDLINE
(5) Metha, S; Journal of Microencapsulation 1996, V13, P269
(6) Metha, S; Pharmaceutical Research 1996, V13, P344
(7) Mishima, Y; Lancet 1989, VII, P388
(8) Mori, Y; Pigment Cell Research 1989, V2, P273 HCAPLUS
(9) New, R; Liposomes:a practical approach 1990, P105
(10) Pidgeon, C; Analytical Biochemistry 1989, V181, P28 HCAPLUS
(11) Pinelli, T; Proceedings of 6th International Symposium on NCT for cancer 1994, P783
(12) Shelly, K; Proceedings of the National Academy of Science, USA 1992, V89, P9039 HCAPLUS
(13) Szoka, F; Biochimica and Biophysics Acta 1980, V601, P559 HCAPLUS
(14) Uchiyama, K; International Journal of Pharmaceutics 1995, V121, P195 HCAPLUS

IT **57-88-5**, Cholesterol, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing **boronophenylalanine** for **boron** neutron capture therapy)
RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L131 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1994:528879 HCAPLUS
DOCUMENT NUMBER: 121:128879
ENTRY DATE: Entered STN: 17 Sep 1994
TITLE: Na3[B20H17NH3]: Synthesis and liposomal delivery to murine tumors
AUTHOR(S): Feakes, Debra A.; Shelly, Kenneth; Knobler, Carolyn B.; Hawthorne, M. Frederick
CORPORATE SOURCE: Dep. Chem. Biochem., Univ. California, Los Angeles, CA, 90024, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1994**), 91(8), 3029-33
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 8-9 (Radiation Biochemistry)
Section cross-reference(s): 14

ABSTRACT:
The polyhedral borane ion [n-B20H18]2- reacts with liquid ammonia in the presence of a suitable base to produce an apical-equatorial (ae) isomer of the [B20H17NH3]3- ion, [1-(2'-B10H9)-2-NH3B10H8]3-. The structure of this product has been confirmed by 11B NMR spectroscopy and x-ray crystallog. This species undergoes acid-catalyzed rearrangement to an apical-apical (a2) isomer, [1-(1'-B10H9)-2-NH3B10H8]3-, whose structure has been determined by 11B NMR spectroscopy. The sodium salts of both the ae and the a2 isomers of [B20H17NH3]3- have been encapsulated within small **unilamellar** liposomes, composed of distearoylphosphatidylcholine/cholesterol (1:1), and investigated as boron-delivery agents for boron neutron capture therapy (BNCT) of cancer. The biodistribution of boron was determined after the injection of liposomal suspensions into BALB/c mice bearing EMT6 tumors. Both [B20H17NH3]3- isomers exhibited excellent tumor uptake and selectivity at very low injected doses, achieving peak tumor boron concns. of 30-40 μg of B/g of tissue and tumor/blood boron ratios of ≈5. The enhanced retention of the [B20H17NH3]3- isomers by EMT6 tumors may be attributed to their facile intracellular oxidation to an extremely reactive NH3-substituted [n-B20H18]2- ion, the electrophilic [B20H17NH3]- ion. Both isomers of [B20H17NH3]3- are at least 0.5 V more easily oxidized than other previously investigated species containing 20 boron atoms. In another experiment, [ae-B20H17NH3]3- was encapsulated in liposomes prepared with 5% PEG-2000-distearoylphosphatidylethanolamine in the liposome membrane. As expected, these liposomes exhibited a longer circulation lifetime in the biodistribution experiment, resulting in the continued accumulation of boron in the tumor over the entire 48-h experiment and reaching a maximum of 47 μg of B/g of tumor.

SUPPL. TERM: liposomal polyhedral borane prepn delivery tumor; boron neutron capture radiotherapy liposomal borane

INDEX TERM: Neoplasm
(liposomal polyhedral borane delivery to, boron-neutron capture radiotherapy in relation to)

INDEX TERM: Pharmaceutical dosage forms
(liposomes, polyhedral borane-containing, preparation and tumor
delivery of, boron-neutron capture radiotherapy in relation to)

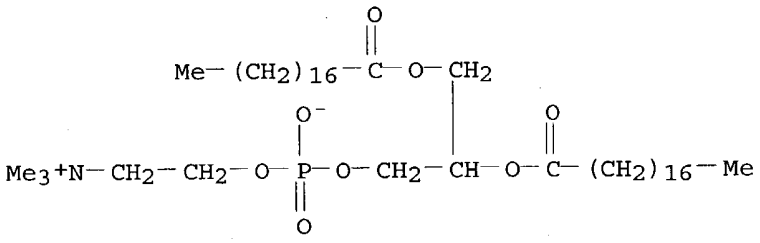
INDEX TERM: **4539-70-2P**, Distearoyl phosphatidylcholine
157143-39-0P 157143-41-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(liposomal, preparation and tumor delivery of, boron-neutron capture radiotherapy in relation to)

INDEX TERM: **57-88-5P**, Cholesterol, biological studies
4537-76-2P, Distearoylphosphatidylethanolamine
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(liposome, polyhedral **borane**-containing, preparation and tumor delivery of, **boron**-neutron capture radiotherapy in relation to)

IT **4539-70-2P**, Distearoyl phosphatidylcholine
RL: SPN (Synthetic preparation); PREP (Preparation)
(liposomal, preparation and tumor delivery of, boron-neutron capture radiotherapy in relation to)

RN 4539-70-2 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

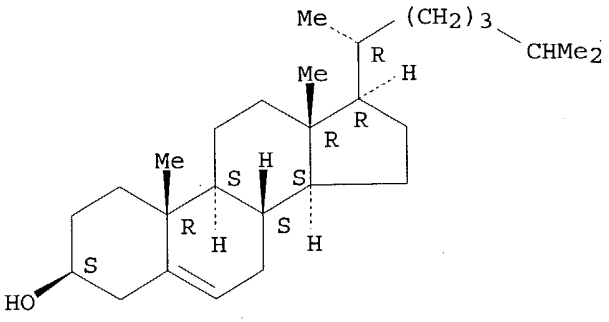


IT **57-88-5P**, Cholesterol, biological studies
RL: SPN (Synthetic preparation); PREP (Preparation)
(liposome, polyhedral **borane**-containing, preparation and tumor delivery of, **boron**-neutron capture radiotherapy in relation to)

RN 57-88-5 HCAPLUS

CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L131 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:593220 HCAPLUS
DOCUMENT NUMBER: 135:170765
ENTRY DATE: Entered STN: 16 Aug 2001
TITLE: Compositions for boron delivery to mammalian tissue
INVENTOR(S): Hawthorne, M. Frederick; Feaks, Debra Arlene; Shelly, Kenneth John
PATENT ASSIGNEE(S): Reagents of the University of California, USA
SOURCE: U.S., 29 pp., Cont.-in-part of U.S. 5,888,473.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.: A61K051-00; A61K091-27
US PATENT CLASSIF.: 424012100
CLASSIFICATION: 63-5 (Pharmaceuticals)
Section cross-reference(s): 8, 29
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6274116	B1	20010814	US 1999-280098	19990329 <--
US 5648532	A	19970715	US 1993-71702	19930603 <--
US 5888473	A	19990330	US 1995-511073	19950803 <--
US 6517808	B1	20030211	US 2001-837147	20010418 <--

PRIORITY APPLN. INFO.: US 1993-71702 A3 19930603 <--
US 1995-511073 A2 19950803 <--
US 1999-280098 A3 19990329 <--
OTHER SOURCE(S): MARPAT 135:170765
ABSTRACT:
Boron neutron capture therapy can utilize XyB20 H17 L where X is an alkali metal, y is 1 to 4, and L is a two electron donor such as NH3, and Na2B10H9NCO, among others. These borane salts may be used free or encapsulated in liposomes. Liposomes may also have embedded within their **bilayers** carboranes to increase the amount of delivered 10B and/or to increase the tumor specificity of the liposome.

SUPPL. TERM: liposome boron compd prepn tumor BNCT
INDEX TERM: NMR (nuclear magnetic resonance)
(boron-11; liposomal compns. for boron delivery to tumors)
INDEX TERM: Radiotherapy
(boron-neutron capture; liposomal compns. for boron delivery to tumors)
INDEX TERM: Antitumor agents

Crystal structure
Neoplasm
(liposomal compns. for boron delivery to tumors)

INDEX TERM: **Phospholipids, uses**
ROLE: MOA (Modifier or additive use); USES (Uses)
(liposomal compns. for boron delivery to tumors)

INDEX TERM: Proteins, general, biological studies
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(liposomal compns. for boron delivery to tumors: reaction with intracellular proteins)

INDEX TERM: Drug delivery systems
(liposomes; liposomal compns. for boron delivery to tumors)

INDEX TERM: 7440-42-8, Boron, biological studies
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(liposomal compns. for boron delivery to tumors)

INDEX TERM: 12294-20-1 144885-51-8 157143-38-9 165178-93-8
165290-42-6 176105-69-4 180907-07-7 213134-11-3
ROLE: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(liposomal compns. for boron delivery to tumors)

INDEX TERM: **57-88-5**, Cholesterol, uses **816-94-4**, DSPC
ROLE: MOA (Modifier or additive use); USES (Uses)
(liposomal compns. for **boron** delivery to tumors)

INDEX TERM: 354134-69-3
ROLE: PRP (Properties)
(liposomal compns. for boron delivery to tumors)

INDEX TERM: 112-89-0 629-89-0, 1-Octadecyne 12075-73-9 12356-22-8
12404-15-8 17702-35-1 17702-41-9, Decaborane(14)
55914-86-8 165178-78-9 165306-81-0
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(liposomal compns. for boron delivery to tumors)

INDEX TERM: 165178-77-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(liposomal compns. for boron delivery to tumors)

INDEX TERM: 141664-81-5P 141684-17-5P 141684-19-7P 164072-14-4P
165178-80-3P 165178-82-5P 165178-83-6P 165178-89-2P
165178-90-5P 165178-92-7P 165306-80-9P 165337-85-9P
354134-72-8P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(liposomal compns. for boron delivery to tumors)

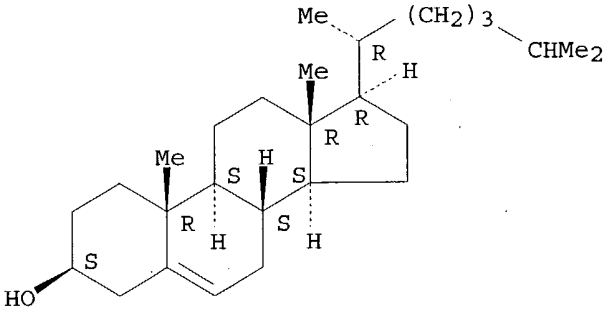
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Anon; WO 9222298 1992 HCAPLUS
(2) Fujii; US 5328678 1994 HCAPLUS
(3) Kane; US 5856551 1999 HCAPLUS
(4) Shelly, K; Proc Natl Acad Sci 1992, V89, P9039 HCAPLUS
(5) Spielvogel; US 5272250 1993 HCAPLUS

IT **57-88-5**, Cholesterol, uses **816-94-4**, DSPC
RL: MOA (Modifier or additive use); USES (Uses)
(liposomal compns. for **boron** delivery to tumors)

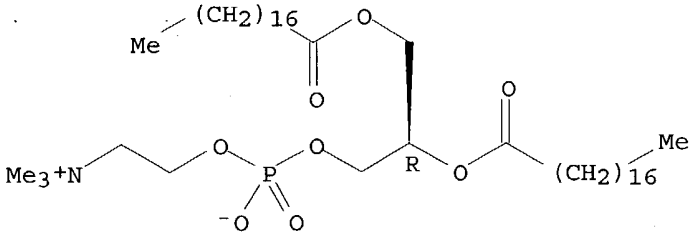
RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 816-94-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L131 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:310719 HCAPLUS
DOCUMENT NUMBER: 138:44571
ENTRY DATE: Entered STN: 25 Apr 2002
TITLE: SLT-particles for two-step targeting in boron neutron capture therapy
AUTHOR(S): Bohl, E.; Carlsson, J.; Edwards, K.; Sjoberg, S.; Gedda, L.
CORPORATE SOURCE: Biomedical Radiation Sciences Rudbeck Laboratory, Uppsala, 75185, Swed.
SOURCE: Frontiers in Neutron Capture Therapy, [Proceedings of the International Symposium on Neutron Capture Therapy for Cancer], 8th, Los Angeles, CA, United States, Sept. 13-18, 1998 (**2001**), Meeting Date 1998, Volume 2, 1069-1075. Editor(s): Hawthorne, M. Frederick; Shelly, Kenneth; Wiersema, Richard J. Kluwer Academic/Plenum Publishers: New York, N. Y. CODEN: 69CMQV; ISBN: 0-306-46442-X
DOCUMENT TYPE: Conference
LANGUAGE: English
CLASSIFICATION: 63-5 (Pharmaceuticals)
Section cross-reference(s): 8

ABSTRACT:
The magnitude of the unspecific cellular uptake of liposome encapsulated boronated DNA intercalators was determined It is essential that the unspecific drug delivery is at a low level to ensure low damage to healthy tissue. The boronated DNA-intercalating agents water-soluble boronated acridine WSA-1 and

water soluble boronated phenanthridine WSP-1 were used in the study. Uptake ***monolayer*** U-343 glioma cells of WSA-1, WSA-1 in stabilized liposomes, WSP-1, and WSP-1 in stabilized liposomes was studied. The binding in DU-145 prostatic spheroids was studied using WSA-1, WSA-1 in stabilized liposomes, WSP-1 and WSP-1 in stabilized liposomes in a concentration of 5μg/mL. The clonogenic survival test showed that after 24 h incubation the liposome encapsulated compds. did exhibit a less toxic behavior than the free compds. The most toxic compound WSP-1 showed a large decrease in survival even at low concns. Since the stabilized liposomes loaded with boronated DNA-intercalating compds. are to be used in two-step targeting the unspecific uptake should be low. It is also very significant that the liposomes are able to penetrate into spheroids since they are to be used in hunting tumors.

SUPPL. TERM: boronated DNA intercalator liposome tumor uptake

INDEX TERM: Intercalation
(agents; tumor cell uptake of liposome-encapsulated DNA-intercalating boron compds.)

INDEX TERM: Radiotherapy
(boron-neutron capture; liposome particles for two-step targeting in boron neutron capture therapy)

INDEX TERM: Neoplasm
Neuroglia, neoplasm
(glioma cell uptake of liposome-encapsulated boron compds.)

INDEX TERM: Drug delivery systems
(liposomes; liposome particles for two-step targeting in boron neutron capture therapy)

INDEX TERM: Human
(tumor cell uptake of liposome-encapsulated DNA-intercalating boron compds.)

INDEX TERM: DNA
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor cell uptake of liposome-encapsulated DNA-intercalating boron compds.)

INDEX TERM: 200135-21-3, WSP-1 206347-16-2, WSA-1
ROLE: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome particles for two-step targeting in boron neutron capture therapy)

INDEX TERM: **57-88-5**, Cholesterol, biological studies
4539-70-2, DSPC 145035-96-7, DSPE-PEG
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome particles for two-step targeting in **boron** neutron capture therapy)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD.

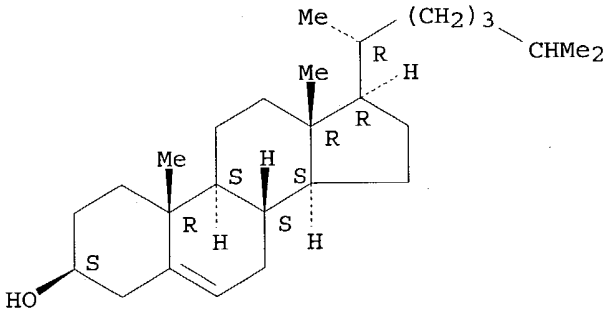
REFERENCE(S):

(1) Allen, T; Biochimia et Biophysica Acta 1995, V1237, P99 HCAPLUS
(2) Feakes, D; Proc Natl Acad Sci USA 1995, V92, P1367 HCAPLUS
(3) Gedda, L; Comprehensive Summaries of Dissertations from the Faculty of Medicine 1997, V724
(4) Ghaneolhosseini, H; Comprehensive summaries of Uppsala Dissertations from the Faculty of Science and Technology 1998, V356
(5) Hartman, T; Radiotherapy and Oncology 1993, V31, P61
(6) Hawthorne, M; Oncology 1997, V33, P53 MEDLINE

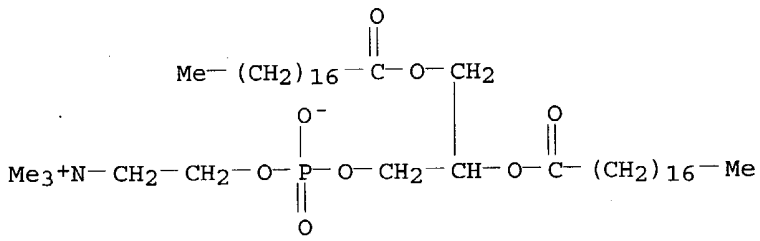
(7) Lindstrom, P; Anti-Cancer Drugs 1994, V5, P43 MEDLINE
(8) Nemoto, H; J Med Chem 1995, V38, P1673 HCAPLUS
(9) Shelly, K; Proc Natl Acad Sci USA 1992, V89, P9039 HCAPLUS
(10) Woodle, M; Advanced Drug Delivery Reviews V16, P249 HCAPLUS

IT **57-88-5**, Cholesterol, biological studies **4539-70-2**, DSPC
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome particles for two-step targeting in **boron** neutron capture therapy)
RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



L131 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:347002 HCAPLUS
DOCUMENT NUMBER: 138:95452
ENTRY DATE: Entered STN: 09 May 2002
TITLE: Tumor cell-selective delivery of boron compounds via folate receptor-targeted liposomes
AUTHOR(S): Pan, X.; Shukla, S.; Sekido, M.; Tjarks, W.; Adams, D.; Barth, R.; Ji, W.; Wang, H.; Shi, G.; Sudimack, J.; Guo, W.; Lee, R. L.
CORPORATE SOURCE: College of Pharmacy, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (**2001**),

Volume 1, 580-581. Controlled Release Society:
Minneapolis, Minn.
CODEN: 69CNY8
DOCUMENT TYPE: Conference
LANGUAGE: English
CLASSIFICATION: 63-6 (Pharmaceuticals)
Section cross-reference(s): 8

ABSTRACT:
Encapsulation efficiency of boron-derivatized polyamine compds. (SPD-5, ASPD-5, ASPM-5, SPM-5,10, and BBSPD-5) in liposomes with four different methods are evaluated. Tumor uptake of boron-containing liposomes in culture KB cells were also studied. The efficiency of boron encapsulation in liposomes is highly dependent on the trapping agent. The use of (NH4)2SO4 as a trapping agent was more effective than usage of citric acid. Folate-PEG-liposomes showed excellent target cell specificity and warrant further evaluation as a carrier for tumor-selective delivery of boron for boron neutron capture therapy (BNCT).

SUPPL. TERM: boron polyamine folate PEG liposome tumor targeting

INDEX TERM: **Radiotherapy**
(boron-neutron capture; encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: **Phosphatidylethanolamines, biological studies**
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates with PEG and folic acid; encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: Polyoxyalkylenes, biological studies
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates with folic acid and PE; encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: **Drug delivery** systems
Encapsulation
Human
Particle size distribution
Radiotherapy
(encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: **Phosphatidylcholines, biological studies**
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: **Drug delivery** systems
(liposomes; encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: Amines, biological studies
ROLE: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); PROC (Process); USES (Uses)
(polyamines, nonpolymeric; encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: Biological transport
(uptake; encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: 12294-22-3 164072-14-4
ROLE: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process)
(encapsulation efficiency of boron-derivatized compds. in liposomes)

INDEX TERM: 165823-32-5P 186037-03-6P 226881-22-7P 226881-23-8P 226881-26-1P
ROLE: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

INDEX TERM: **57-88-5**, Cholesterol, biological studies 59-30-3, Folic acid, biological studies 59-30-3D, Folic acid, conjugates with PEG and PE 25322-68-3D, PEG, conjugates with folic acid and PE 27321-96-6
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation efficiency of **boron**-derivatized compds. in liposomes and tumor uptake of **boron**-containing liposomes for **boron** neutron capture therapy)

INDEX TERM: 77-92-9, Citric acid, biological studies 7783-20-2, Ammonium sulfate ((NH4)2SO4), biological studies
ROLE: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trapping agent; encapsulation efficiency of boron-derivatized compds. in liposomes and tumor uptake of boron-containing liposomes for boron neutron capture therapy)

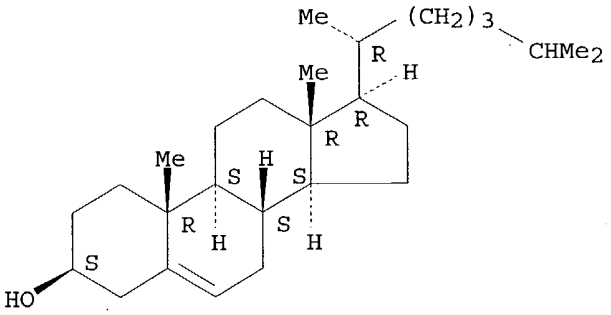
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Johnsson; J Liposome Res 1999, V9, P53 HCAPLUS
(2) Lee; Biol Chem 1994, V269, P3198 HCAPLUS
(3) Soloway; Chem Rev 1998, V98, P1515 HCAPLUS

IT **57-88-5**, Cholesterol, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation efficiency of **boron**-derivatized compds. in liposomes and tumor uptake of **boron**-containing liposomes for **boron** neutron capture therapy)

RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L131 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:18290 HCAPLUS
DOCUMENT NUMBER: 135:247084
ENTRY DATE: Entered STN: 09 Jan 2001
TITLE: Preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivatives of cholesterol
AUTHOR(S): Feakes, Debora A.; Tate, Colby C.; Stefanutti, Sara J.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Southwest Texas State University, San Marcos, TX, 78666, USA
SOURCE: KURRI-KR (**2000**), KURRI-KR-54, 155-156
CODEN: KURRBF; ISSN: 1342-0852
DOCUMENT TYPE: Report
LANGUAGE: English
CLASSIFICATION: 63-5 (Pharmaceuticals)
ABSTRACT:
The application of boron neutron capture therapy is dependent on the identification and preparation of boron-containing compds. that can be delivered and retained by the tumor cells. **Unilamellar liposomes** have been investigated as potential tumor-specific delivery vehicles for boron-containing compds. that have no inherent tumor specificity. A series of carborane-containing derivs. of cholesterol have been prepared and incorporated into the **bilayer** of **unilamellar liposomes.** The cholesterol derivs. vary in the linker moiety (ester and ether), the chain length between the cholesterol and the carborane substituent, and the identity of the carborane group itself (closo- and nido-). The ability of the boron-containing derivs. of cholesterol to be incorporated into the **bilayer** of the **unilamellar liposomes** and the stability of the resulting **liposome** formulations will be presented.

SUPPL. TERM: cholesterol carborone contg deriv **liposome** BNCT
INDEX TERM: Radiotherapy
(boron-neutron capture; preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivs. of cholesterol)
INDEX TERM: Drug delivery systems
(**liposomes**; preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivs. of cholesterol)
INDEX TERM: Drug targeting
(preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivs. of cholesterol)
INDEX TERM: Carboranes
ROLE: RCT (Reactant); RACT (Reactant or reagent)

(preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivs. of cholesterol)

INDEX TERM: **249903-49-9P 359851-17-5P**
ROLE: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivs. of cholesterol)

INDEX TERM: **816-94-4**, DSPC
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivs. of cholesterol)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD.

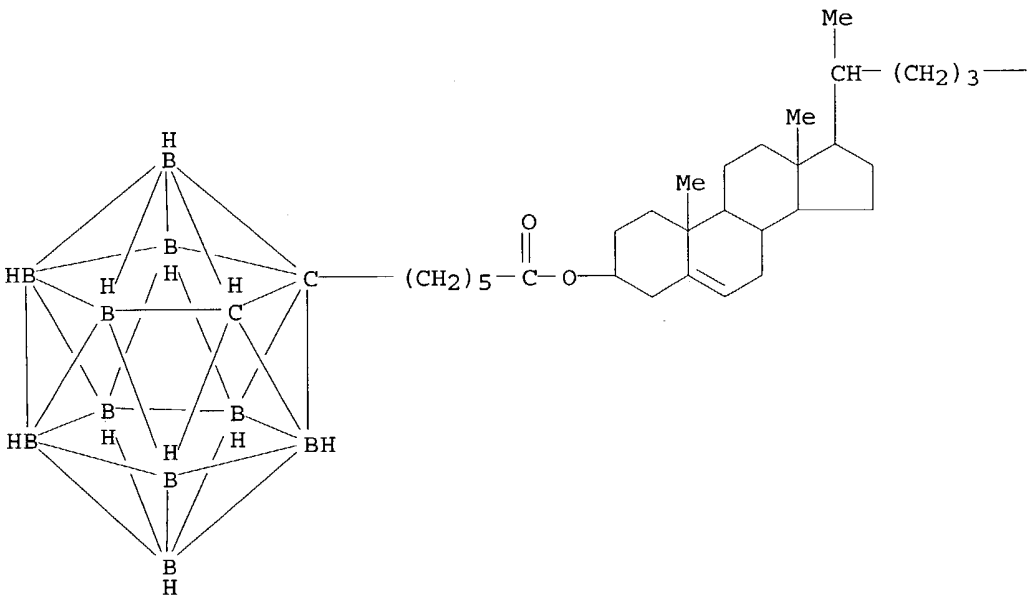
REFERENCE(S):

(1) Clendonen, N; Neurosurgery 1990, V26, P47
(2) Coderre, J; Cancer Res 1988, V48, P6313 HCAPLUS
(3) Deamer, D; Liposomes 1983, P31
(4) Feakes, D; Proc Natl Acad Sci USA 1994, V91, P3029 HCAPLUS
(5) Feakes, D; Proc Natl Acad Sci USA 1995, V92, P1367 HCAPLUS
(6) Feakes, D; Proc Natl Acad Sci USA 1999, V96, P6406 HCAPLUS
(7) Feakes, D; Tetrahedron 1999, V55, P11177 HCAPLUS
(8) Fraley, R; Biochemistry 1981, V20, P6978 HCAPLUS
(9) Gabel, D; Cancer Res 1987, V47, P5451 HCAPLUS
(10) Proffitt, R; J Nucl Med 1983, V24, P45 HCAPLUS
(11) Shelly, K; Proc Natl Acad Sci USA 1992, V89, P9039 HCAPLUS
(12) Slatkin, D; Biochem Pharmacol 1986, V35, P1771 HCAPLUS
(13) Soloway, A; Medicinal Chem 1967, V10, P714 HCAPLUS
(14) Straubinger, R; Biochemistry 1990, V29, P4929 HCAPLUS
(15) Straubinger, R; Cell 1983, V32, P1069 HCAPLUS
(16) Sweet, W; J Pharmacol Exp Ther 1962, V137, P263 HCAPLUS
(17) Tamat, S; Anal Chem 1987, V59, P2161 HCAPLUS
(18) Wallingford, R; J Nucl Med 1985, V26, P1180 HCAPLUS

IT **249903-49-9P 359851-17-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivs. of cholesterol)

RN 249903-49-9 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, 6-(1,2-dicarbadodecaboran(12)-1-yl)hexanoate (9CI) (CA INDEX NAME)

PAGE 1-A

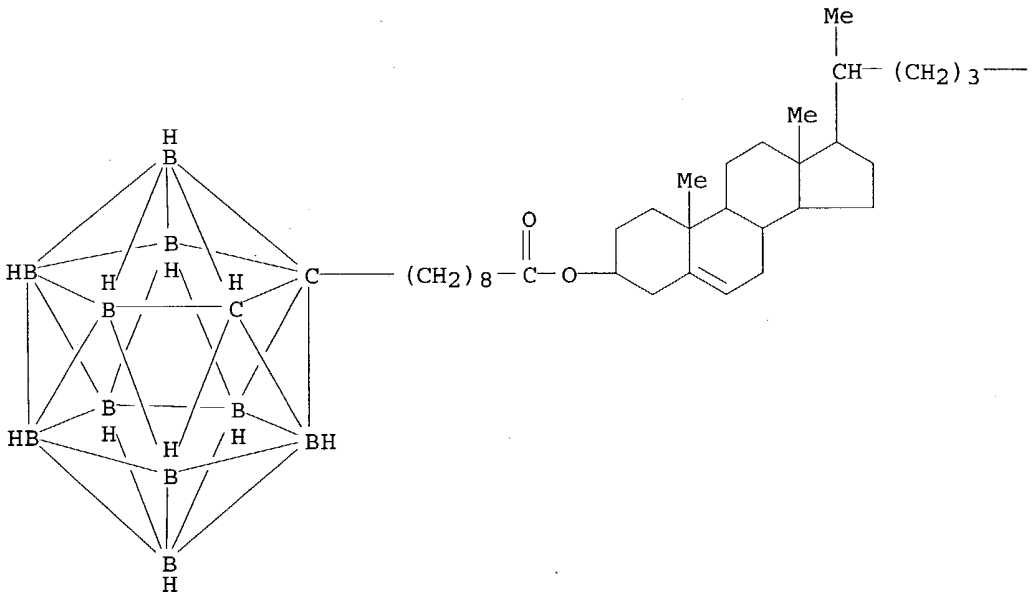


PAGE 1-B

— $CHMe_2$

RN 359851-17-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)-, 9-(1,2-dicarbadodecaboran(12)-1-yl)nonanoate (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

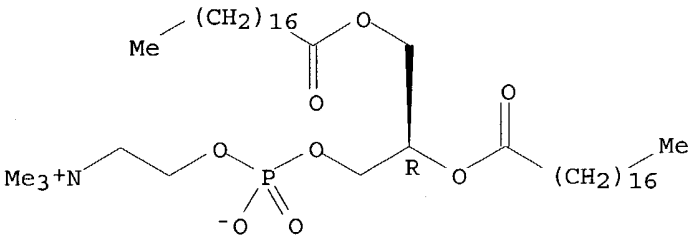
— $CHMe_2$

IT **816-94-4**, DSPC
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and evaluation of **unilamellar liposomes** incorporating boron-containing derivs. of cholesterol)

RN 816-94-4 HCAPLUS

CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L131 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:404815 HCAPLUS
DOCUMENT NUMBER: 131:56154
ENTRY DATE: Entered STN: 01 Jul 1999
TITLE: Optoacoustic contrast agents and methods for their use in ultrasound and optical imaging
INVENTOR(S): Unger, Evan C.; Wu, Yunqiu
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61B008-13
SECONDARY: A61K049-00
CLASSIFICATION: 9-16 (Biochemical Methods)
Section cross-reference(s): 8, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930620	A1	19990624	WO 1998-US27060	19981217 <--
W: AU, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6123923	A	20000926	US 1997-993165	19971218 <--
AU 9919318	A1	19990705	AU 1999-19318	19981217 <--
EP 1039834	A1	20001004	EP 1998-964127	19981217 <--
R: DE, FR, GB, IT				

PRIORITY APPLN. INFO.: US 1997-993165 A 19971218 <--
WO 1998-US27060 W 19981217 <--

ABSTRACT:
The present invention generally relates to optoacoustic contrast agents and methods of diagnostic and therapeutic imaging using optoacoustic contrast agents. A composition comprising a stabilizing material and a photoactive agent is administered and the patient is scanned using ultrasound imaging and optical imaging to obtain visible images of a region of the patient. The compns. may comprise a wide variety of addnl. components, including, for example, one or more of gases, gaseous precursors, liqs. oils, stabilizing materials, diagnostic agents, photoactive agents, bioactive agents, and/or targeting ligands. Perfluoropropane encapsulated optoacoustic **liposomes** were formed from dipalmitoylphosphatidylcholine, dipalmitoylphosphatidic acid, dipalmitoylphosphatidylethanolamine-PEG 5,000, and dipalmitoylphosphatidylethanolamine derivatized with lissamine rhodamine B. The sized photoactive **lipid** was optimally excited with 550 nm light and the fluorescence emission peak was 590 nm.

SUPPL. TERM: optoacoustic contrast agent optical ultrasound imaging; **liposome** perfluoropropane lissamine rhodamine B optoacoustic contrast agent
INDEX TERM: **Imaging**
(acoustic; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)
INDEX TERM: Nucleic acids
Oligodeoxyribonucleotides
ROLE: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(antigene, as targeting ligand, composition further containing;

optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Cyanine dyes
Fluorescent substances
Photosensitizers (**pharmaceutical**)
(as photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Bile pigments
Biliproteins
Carotenes, biological studies
Flavonoids
Fullerenes
Metalloporphyrins
Phycocyanins
Phycoerythrins
Phytochromes
Porphyrins
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Proteins, general, biological studies
ROLE: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(as stabilizer or targeting ligand; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Surfactants
(as stabilizer; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: **Lipids**, biological studies
Polymers, biological studies
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as stabilizer; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Antibodies
Antisense DNA
Antisense RNA
Antisense oligonucleotides
Carbohydrates, biological studies
DNA
Gene, animal
Glycolipids
Lipoproteins
Oligonucleotides
Peptides, biological studies
RNA
Ribozymes
ROLE: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(as targeting ligand, composition further containing; optoacoustic
contrast agents and methods for their use in ultrasound

and optical imaging)

INDEX TERM: Porphyrins
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(benzoporphyrins, as photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Porphyrins
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(chlorins, as photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Gases
(composition further containing gaseous precursor and or; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Drugs
(composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Perfluorocarbons
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Polyenes
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(conjugated, as photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Antibodies
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(conjugates, with photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Unsaturated compounds
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cyanines, as photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Disease, animal
(diagnosis of; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: **Phosphatidylethanolamines, biological studies**
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(fluorescein conjugates, perfluorobutane encapsulated in optoacoustic **liposomes** containing; optoacoustic

contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Liquids
(fluorinated, composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Surfactants
(fluorosurfactants, as stabilizer; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: RNA
Ribozymes
ROLE: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(hammerhead, as targeting ligand, composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: **Diagnosis**
(of diseased tissue; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Liquids
(oils, composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: **Imaging**
Neoplasm
Sound and Ultrasound
Stabilizing agents
(optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: **Imaging** agents
(optoacoustic contrast agents; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Thrombus
(optoacoustic **liposomes** targeting; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Perfluoro compounds
Perfluoro compounds
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(perfluoroalkyl ethers, composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Ethers, biological studies
Ethers, biological studies
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(perfluoroalkyl, composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Materials
(photoactive chems.; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Solids
(porous matrix; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Interleukin 2
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of targeting optoacoustic contrast agent for thrombus; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Thrombolytics
(targeting optoacoustic **liposomes** for; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: Ligands
ROLE: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(targeting, composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: 106-60-5, δ-Aminolevulinic acid 302-79-4, Retinoic acid 302-79-4D, Retinoic acid, derivs. 479-61-8 553-12-8, Protoporphyrin IX 574-93-6D, Phthalocyanine, derivs. 603-34-9D, Triphenylamine, derivs. 643-79-8, o-Phthaldialdehyde 917-23-7D, Tetraphenylporphine, sulfonated derivs. 1075-06-5, Phenylglyoxal monohydrate 1210-12-4, 9-Anthronitrile 2321-07-5D, Fluorescein, derivs. 3599-32-4, Indocyanine green 5143-18-0 7149-49-7, Naphthalene-2,3-dicarboxaldehyde 12713-07-4D, Verdin, derivs. 12778-00-6, Mesochlorin 13558-31-1D, derivs. 14325-05-4, Tin protoporphyrin 14459-29-1, Hematoporphyrin 19660-77-6, Chlorin e6 19660-77-6D, Chlorin e6, mono-L-aspartyl derivative 23627-89-6D, Naphthalocyanine, derivs. 25440-13-5 26038-83-5, 4-Heptadecyl-7-hydroxycoumarin 41085-99-8 41387-42-2 60415-70-5D, 21H,23H-Porphin-5(22H)-one, derivs. 61494-52-8, 1-Pyrenesulfonyl chloride 62796-29-6, Lissamine rhodamine B sulfonyl chloride 62888-19-1, Bonellin 65603-18-1 65603-19-2, Octadecyl rhodamine B chloride 68335-15-9, Photofrin 72467-67-5 72535-39-8 73024-99-4, 12-(9-Anthroyloxy)oleic acid 75168-11-5 76081-97-5, Cholesteryl 1-pyrenebutyrate 78949-95-8 88235-25-0 88478-07-3 95864-17-8 96886-70-3 97850-83-4, Cholesteryl 1-pyrenedecanoate 99128-91-3, Octaethylpurpurin 100572-96-1D, Porphycene, compds. 105344-74-9 113471-15-1 114041-00-8 114494-17-6 114586-25-3 115645-42-6 123738-53-4 123940-54-5, Hypocrellin B 128146-77-0 134020-79-4D, Sapphyrin, derivs. 135615-37-1D, Rubyrin, derivs. 138026-68-3 147662-88-2, 2-Dodecylresorufin **151736-99-1** 151892-94-3 186833-02-3 216434-81-0 217187-10-5 227936-56-3D, 2λ4-1,2,5-Oxatellurazole, derivs. 227936-57-4
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: 75-73-0 76-16-4 76-19-7, Perfluoropropane 115-25-3, Perfluorocyclobutane 306-94-5, Perfluorodecalin 307-34-6, Perfluorooctane 307-45-9, Perfluorodecane 307-59-5, Perfluorododecane 311-89-7, Perfluorotributylamine 335-57-9, Perfluoroheptane 338-83-0, Perfluorotripropylamine 355-25-9, Perfluorobutane 355-42-0, Perfluorohexane 355-68-0, Perfluorocyclohexane 355-79-3, Perfluorotetrahydropyran 356-62-7, Bis(perfluoropropyl) ether 358-21-4, Perfluorodiethyl ether 375-03-1, Perfluoropropylmethyl ether 375-96-2, Perfluorononane 376-77-2, Perfluorocyclopentane 423-55-2, Perfluorooctylbromide 507-63-1, Perfluorooctyliodide 665-16-7, Perfluoromethylethyl ether 678-26-2, Perfluoropentane 931-91-9, Perfluorocyclopropane 1479-49-8, Perfluorodimethyl ether 2551-62-4, Sulfur hexafluoride 13782-76-8, Perfluorobutylethyl ether 19448-33-0 51001-25-3D, perfluoro 66840-50-4 83935-39-1, Bis(perfluoroisopropyl) ether 163702-07-6, Perfluorobutylmethyl ether 199171-52-3 199171-53-4
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(composition further containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: 10199-89-0
ROLE: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(conjugates with diacylphosphatidyl ethanolamine, thrombus targeting optoacoustic **liposomes** containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: 186750-18-5P 186750-19-6P 186750-20-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in preparation of targeting optoacoustic contrast agent for thrombus; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: **2644-64-6**, Dipalmitoylphosphatidylcholine
19698-29-4, Dipalmitoylphosphatidic acid
145035-97-8
ROLE: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(perfluoropropane encapsulated in optoacoustic **liposomes** containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

INDEX TERM: 186750-20-9DP, conjugates with interleukin 2
ROLE: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of, as targeting optoacoustic contrast agent for thrombus; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

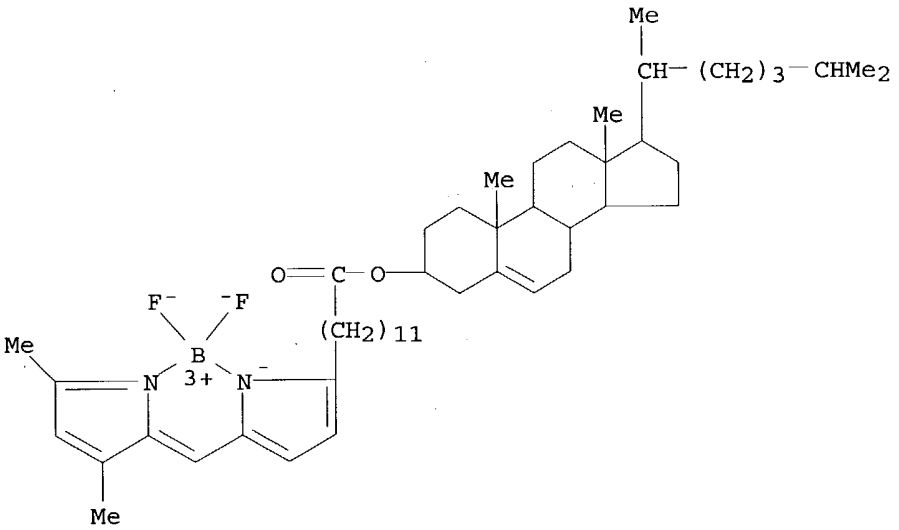
INDEX TERM: 6066-82-6, N-Hydroxysuccinimide 108032-13-9 139729-28-5
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of targeting optoacoustic contrast agent for thrombus; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):
(1) Levy; US 5283255 A 1994 HCAPLUS
(2) Nakakjima, S; Proc SPIE-Int Soc Opt Eng 1995, V2371, P495 HCAPLUS
(3) Unger; US 5846517 A 1998 HCAPLUS
(4) Walters; US 5460800 A 1995
(5) Warren, S; Proc Int Conf Lasers 1993, V15, P795

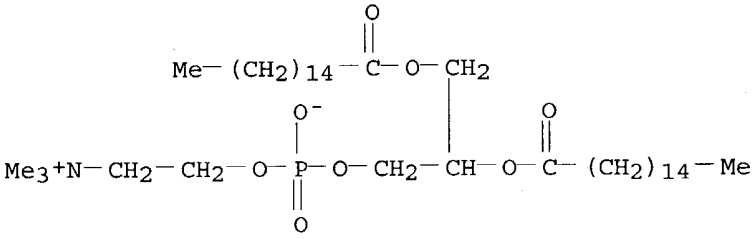
IT **151736-99-1**
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as photoactive agent; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

RN 151736-99-1 HCAPLUS
CN Boron, [(3β)-cholest-5-en-3-yl 5-[(3,5-dimethyl-2H-pyrrol-2-ylidene)methyl]-1H-pyrrole-2-dodecanoato-κN1,κN5]difluoro-, (T-4)- (9CI) (CA INDEX NAME)

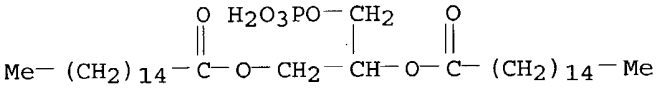


IT **2644-64-6**, Dipalmitoylphosphatidylcholine **19698-29-4**, Dipalmitoylphosphatidic acid
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(perfluoropropane encapsulated in optoacoustic **liposomes** containing; optoacoustic contrast agents and methods for their use in ultrasound and optical imaging)

RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 19698-29-4 HCAPLUS
CN Hexadecanoic acid, 1-[(phosphonooxy)methyl]-1,2-ethanediyl ester (9CI) (CA INDEX NAME)



L131 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:570665 HCAPLUS
DOCUMENT NUMBER: 131:314159
ENTRY DATE: Entered STN: 09 Sep 1999
TITLE: Preparation and characterization of liposomal systems entrapping the boronated compound o-carboranylpropylamine
AUTHOR(S): Moraes, A. M.; Santana, M. H. A.; Carbonell, R. G.
CORPORATE SOURCE: Department Processos Biotechnologicos/FEQ/State University of Campinas (UNICAMP), Campinas, 13081-970, Brazil
SOURCE: Journal of Microencapsulation (**1999**), 16(5), 647-664
CODEN: JOMIEF; ISSN: 0265-2048
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 63-6 (Pharmaceuticals)
Section cross-reference(s): 8

ABSTRACT:
Boron neutron capture therapy (BNCT) is based on the nuclear reaction that occurs when the stable isotope, 10B, is irradiated with low-energy thermal neutrons to yield ionizing helium and lithium ions that are highly damaging and usually lethal to cells. The successful treatment of cancer by BNCT requires the selective concentration of 10B within malignant tumors. Liposomes have been used
as therapeutic compound delivery vehicles for in vivo application, including several anticancer agents. The ability of the boron-containing compound, o-carboranylpropylamine chloride, to accumulate within **unilamellar** liposomes in response to a transmembrane pH gradient was evaluated. Characterization of the systems obtained was performed for conventional and polyethylene glycol (PEG)-modified (stealth) liposomes, in terms of lipid and CPA contents, vesicle size and stability in detergent solns. CPA loading and vesicle stability can be controlled by the exptl. procedure. The loading of CPA into liposomes with average diams. of 100 nm was estimated at 13 000 mols./vesicle
for the most stable systems. CPA toxicity to normal human peripheral blood

lymphocytes and to adherent glioblastoma SK-MG-1 cells in vitro decreased as a result of the entrapment of CPA in liposomes.

SUPPL. TERM: liposome entrapment carboranylpropylamine; boron neutron capture therapy liposome; brain glioblastoma carboranylpropylamine liposome

INDEX TERM: Radiotherapy
(boron-neutron capture; preparation and characterization of liposomal systems entrapping carboranylpropylamine)

INDEX TERM: Neuroglia
(glioblastoma; preparation and characterization of liposomal systems entrapping carboranylpropylamine)

INDEX TERM: Drug delivery systems
(liposomes; preparation and characterization of liposomal systems entrapping carboranylpropylamine)

INDEX TERM: Brain, neoplasm
Encapsulation
Lymphocyte
(preparation and characterization of liposomal systems entrapping carboranylpropylamine)

INDEX TERM: 140662-87-9
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation and characterization of liposomal systems entrapping carboranylpropylamine)

INDEX TERM: **57-88-5**, Cholesterol, biological studies
4539-70-2, DSPC 20255-95-2,
Dimyristoylphosphatidylethanolamine 211733-74-3
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and characterization of liposomal systems entrapping **carboranylpropylamine**)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S):

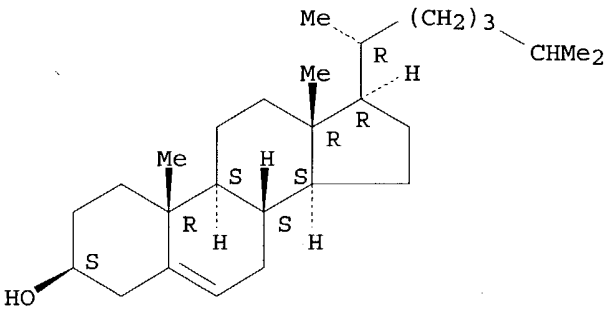
(1) Autry, S; Advances in Neutron Capture Therapy 1997, VII, P347
(2) Barth, R; Cancer 1992, V70, P2995 MEDLINE
(3) Barth, R; Cancer Research 1990, V50, P1061 HCAPLUS
(4) Blume, G; Biochimica et Biophysica Acta 1990, V1029, P91 HCAPLUS
(5) Chen, P; Analytical Chemistry 1956, V28, P1756 HCAPLUS
(6) Edwards, K; Progress in Colloid & Polymer Science 1990, V82, P190 HCAPLUS
(7) Feakes, D; Proceedings of the National Academy of Science 1994, V91, P3029 HCAPLUS
(8) Feakes, D; Proceedings of the National Academy of Science 1995, V92, P1367 HCAPLUS
(9) Ford, N; Dynamic Light Scattering:Applications of Photon Correlation Spectroscopy 1985, P7
(10) Gabizon, A; Proceedings of the National Academy of Science USA 1988, V85, P6949 HCAPLUS
(11) Hall, I; Journal of Pharmaceutical Sciences 1985, V74, P755 HCAPLUS
(12) Hawthorne, F; Angewandte Chemie (International Edition in English) 1993, V32, P959
(13) Klibanov, A; FEBS Letters 1990, V268, P235 HCAPLUS
(14) Lasic, D; Biochimica et Biophysica Acta 1991, V1070, P187 HCAPLUS

(15) Locher, H; American Journal of Roentgenological Radium Therapy 1936, V36, P1
(16) Macdonald, R; Biochemica et Biophysica Acta 1991, V1061, P297 MEDLINE
(17) Madden, T; Chemistry and Physics of Lipids 1990, V53, P37 HCAPLUS
(18) Mayer, L; Biochimical et Biophysica Acta 1990, V1025, P143 HCAPLUS
(19) Mayer, L; Chemistry and Physics of Lipids 1986, V40, P333 HCAPLUS
(20) Mehta, S; Journal of Microencapsulation 1996, V13, P269 HCAPLUS
(21) Moraes, A; Biofunctional Membranes 1996, P229
(22) Murthy, K; Journal of Pharmaceutical Sciences 1970, V59, P1281 HCAPLUS
(23) Papahadjopoulos, D; Proceedings of the National Academy of Science USA 1991, V88, P11460 HCAPLUS
(24) Shelly, K; Proceedings of the National Academy of Science USA 1992, V89, P9039 HCAPLUS
(25) Steffen, D; Master's Thesis, Department of Chemical Engineering, NCSU Raleigh 1993
(26) Szoka, F; Annual Reviews in Biophysics and Bioengineering 1980, V9, P467 HCAPLUS
(27) Woodle, M; Biophysical Journal 1992, V61, P902 HCAPLUS
(28) Wu, N; Cancer Research 1993, V53, P3765 HCAPLUS
(29) Yanagie, H; The British Journal of Cancer 1991, V63, P522 MEDLINE

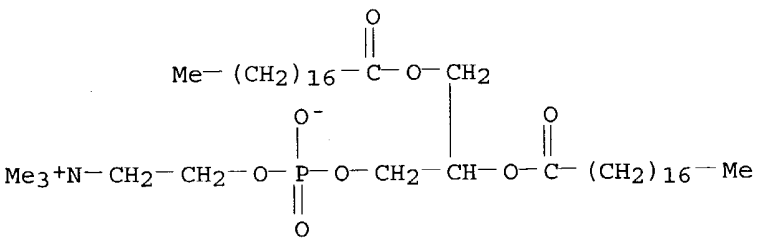
IT **57-88-5**, Cholesterol, biological studies **4539-70-2**, DSPC
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and characterization of liposomal systems entrapping **carboranylpropylamine**)

RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



L131 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:253141 HCAPLUS
DOCUMENT NUMBER: 131:78261
ENTRY DATE: Entered STN: 26 Apr 1999
TITLE: Optimization of drug loading procedures and characterization of liposomal formulations of two novel agents intended for boron neutron capture therapy (BNCT)
AUTHOR(S): Johnsson, Markus; Bergstrand, Nill; Edwards, Katarina
CORPORATE SOURCE: Department of Physical Chemistry, Uppsala University, Uppsala, S-75121, Swed.
SOURCE: Journal of Liposome Research (**1999**), 9(1), 53-79
CODEN: JLREE7; ISSN: 0898-2104
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 63-5 (Pharmaceuticals)
ABSTRACT:
The characterization of 2 liposomal formulations of boronated DNA-interacting agents was performed. The 2 boronated drugs, WSA-Water Soluble Acridine and WSP-Water Soluble Phenantridine, were encapsulated within **unilamellar** sterically stabilized liposomes with high drug-to-lipid ratios (up to 0.50:1 (mol:mol)), using transmembrane pH gradients. The steric stabilization of the liposomes was accomplished by the addition of DSPE-PEG(2000) (PEG-lipid) to DSPC/Cho lipid mixts. and the composition used was DSPC:Cho:DSPE-PEG 55:40:5 (mol%). The loading of the drugs resulted in drug precipitation in the liposomal aqueous ***core*** as observed by cryo-transmission electron microscopy. When pH gradients across the **bilayer** were used for remote loading of WSP or when ammonium sulfate gradients were used for remote loading of WSA, the formation of small **bilayer** fragments (disks) was induced. We present compelling evidence that the formation of disks is a consequence of precipitate growth in the liposomal interior. The precipitate growth causes some of the liposomes to rupture resulting in the above mentioned disk-formation and a substantial decrease in trapping efficiency. The in vitro stability of the drug loaded liposomes was excellent, both in buffer and in 25% human serum. For most of the formulations, the release of the drugs was below or around 10% after 24 h at 37°. The influence of initial internal pH and internal buffering capacity on release properties of WSA and WSP were investigated. The release profiles of the drugs can be controlled, to a large extent, by varying the composition of the internal liposomal aqueous phase.

SUPPL. TERM: liposome drug boron neutron capture therapy
INDEX TERM: Radiotherapy
(boron-neutron capture; optimization and characterization of liposomal formulations of drugs intended for boron

neutron capture therapy)

INDEX TERM: Drug delivery systems
(liposomes, **unilamellar**; optimization and characterization of liposomal formulations of drugs intended for boron neutron capture therapy)

INDEX TERM: Blood serum
Dissolution rate
Encapsulation
(optimization and characterization of liposomal formulations of drugs intended for boron neutron capture therapy)

INDEX TERM: 200135-21-3 229173-99-3
ROLE: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(optimization and characterization of liposomal formulations of drugs intended for boron neutron capture therapy)

INDEX TERM: **57-88-5**, Cholesterol, biological studies
816-94-4, DSPC 9002-92-0, Polyoxyethylene lauryl ether 170931-04-1
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization and characterization of liposomal formulations of drugs intended for **boron** neutron capture therapy)

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD.

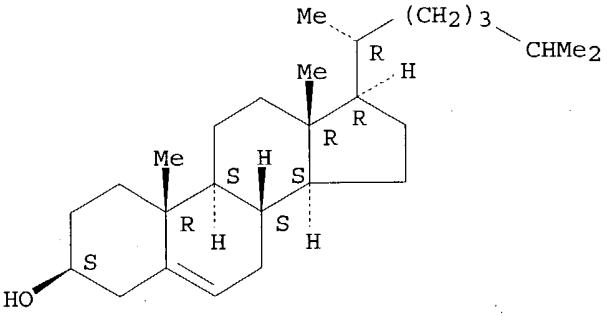
REFERENCE(S):

(1) Allen, T; Biochim Biophys Acta 1991, V1066, P29 HCAPLUS
(2) Amselem, S; J Pharm Sci 1990, V79, P1045 HCAPLUS
(3) Bakker-Woudenberg, I; J Infect Dis 1993, V168, P164
(4) Bellare, J; J Electron Microsc Tech 1988, V10, P87 MEDLINE
(5) Bligh, E; Can J Biochem Physiol 1959, V37, P911 HCAPLUS
(6) Blume, G; Biochim Biophys Acta 1990, V1029, P91 HCAPLUS
(7) Blume, G; Biochim Biophys Acta 1993, V1146, P157 HCAPLUS
(8) Boman, N; Biochim Biophys Acta 1993, V1152, P253 HCAPLUS
(9) Cai, J; Tetrahedron Lett 1996, V37, P9283 HCAPLUS
(10) Ceh, B; Adv Drug Del Rev 1997, V24, P165 HCAPLUS
(11) Ceh, B; J Colloid Interface Sci 1997, V185, P9 HCAPLUS
(12) Ceh, B; Langmuir 1995, V11, P3356 HCAPLUS
(13) Chen, C; Bioconjug Chem 1994, V5, P557 HCAPLUS
(14) Chen, W; Adv Drug Del Rev 1997, V26, P231 HCAPLUS
(15) Crenshaw, J; Biochemistry 1995, V34, P13682 HCAPLUS
(16) Cullis, P; Med Sci Res 1990, V18, P87 HCAPLUS
(17) Denny, W; J Med Chem 1982, V25, P276 HCAPLUS
(18) Dubochet, J; Q Rev Biophys 1988, V21, P129 MEDLINE
(19) Edwards, K; Biophys J 1997, V73, P258 HCAPLUS
(20) Edwards, K; J Colloid Interface Sci 1993, V161, P299 HCAPLUS
(21) Edwards, K; Langmuir 1992, V8, P824 HCAPLUS
(22) Edwards, K; Progr Colloid Polym Sci 1990, V82, P190 HCAPLUS
(23) Feakes, D; Proc Natl Acad Sci 1994, V91, P3029 HCAPLUS
(24) Forssen, E; Cancer Res 1992, V52, P3255 HCAPLUS
(25) Fromherz, P; Chem Phys Lett 1983, V94, P259 HCAPLUS
(26) Fry, D; Anal Biochem 1978, V90, P809 HCAPLUS
(27) Gabel, D; Radiat Res 1987, V111, P14 HCAPLUS
(28) Gabizon, A; Cancer Res 1990, V50, P6371 HCAPLUS
(29) Gedda, L; Bioconjug Chem 1996, V7, P584 HCAPLUS

(30) Gedda, L; Manuscript in preparation 1998
(31) Ghaneolhosseini, H; Tetrahedron 1997, V53, P17519 HCAPLUS
(32) Ghaneolhosseini, H; Tetrahedron 1998, V54, P3877 HCAPLUS
(33) Haran, G; Biochim Biophys Acta 1993, V1151, P201 HCAPLUS
(34) Harrigan, P; Biochim Biophys Acta 1993, V1149, P329 HCAPLUS
(35) Hartman, T; Radiother Oncol 1994, V31, P61 HCAPLUS
(36) Hawthorne, M; Angew Chem Int Ed Engl 1993, V32, P950
(37) Hawthorne, M; J Neuro-Oncology 1997, V33, P53 MEDLINE
(38) Lasic, D; Biochim Biophys Acta 1982, V692, P501 HCAPLUS
(39) Lasic, D; Biochim Biophys Acta 1995, V1239, P145 HCAPLUS
(40) Lasic, D; FEBS LETT 1992, V312, P255 HCAPLUS
(41) Laster, B; Cancer Res 1991, V51, P4588 HCAPLUS
(42) Lelkes, P; Biochim Biophys Acta 1984, V775, P395 HCAPLUS
(43) Lerman, L; J Mol Biol 1961, V3, P18 HCAPLUS
(44) Madden, T; Chem Phys Lip 1990, V53, P37 HCAPLUS
(45) Mayer, L; Biochim Biophys Acta 1985, V816, P294 HCAPLUS
(46) Mayer, L; Biochim Biophys Acta 1990, V1025, P143 HCAPLUS
(47) Mehta, S; J Microencapsulation 1996, V13, P269 HCAPLUS
(48) Oku, N; Biochim Biophys Acta 1992, V1126, P255 HCAPLUS
(49) Papahadjopoulos, D; Proc Natl Acad Sci 1991, V88, P11460 HCAPLUS
(50) Ruiz, J; Biochim Biophys Acta 1988, V937, P127 HCAPLUS
(51) Silvander, M; Accepted for publication in Chem Phys Lip 1998
(52) Silvander, M; Anal Biochem 1996, V242, P40 HCAPLUS
(53) Sobell, H; J Mol Biol 1977, V114, P333 HCAPLUS
(54) Stewart, J; Anal Biochem 1980, V104, P10 HCAPLUS
(55) Ueno, M; Biochemistry 1989, V28, P5631 HCAPLUS
(56) Uster, P; FEBS LETT 1996, V386, P243 HCAPLUS
(57) Wakelin, L; Mol Pharm 1974, V9, P544
(58) Waring, M; Nature 1968, V219, P1320 HCAPLUS
(59) Webb, M; Br J Cancer 1995, V72, P896 HCAPLUS
(60) Woodle, M; Biochim Biophys Acta 1992, V1113, P171 HCAPLUS
(61) Yanagie, H; Br J Cancer 1991, V63, P522 MEDLINE

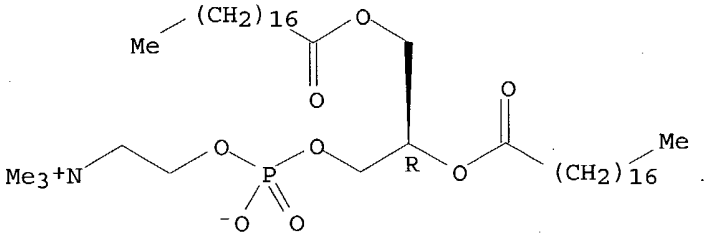
IT **57-88-5**, Cholesterol, biological studies **816-94-4**, DSPC
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(optimization and characterization of liposomal formulations of drugs intended for **boron** neutron capture therapy)
RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 816-94-4 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide, (7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L131 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:289238 HCAPLUS
DOCUMENT NUMBER: 124:352448
ENTRY DATE: Entered STN: 16 May 1996
TITLE: Liposomal formulations containing sodium mercaptoundecahydrododecaborate (BSH) for boron neutron capture therapy
AUTHOR(S): Mehta, S. C.; Lai, J. C. K.; Lu, D. R.
CORPORATE SOURCE: Dep. Pharmaceutics, College Pharmacy, Univ. Georgia, Athens, GA, 30602, USA
SOURCE: Journal of Microencapsulation (**1996**), 13(3), 269-279
CODEN: JOMIEF; ISSN: 0265-2048
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 63-5 (Pharmaceuticals)
Section cross-reference(s): 8

ABSTRACT:
Sodium mercaptoundecahydrododecaborate or BSH is a compound most widely used for boron neutron capture therapy (BNCT). Liposome formulations containing BSH, with or without steric stabilization, were prepared as potential agents for delivery of boron compds. for BNCT. Liposomes composed of DPPC/CHOL in a molar ratio 1:1 (PEG concentration: 5 mol%) were prepared having an average diameter in the range of
100-110 nm 200 μL of liposomes (1.88 mg phospholipid/mouse and 3.5-5.8 mg BSH/kg body weight) were injected in mice via the tail vein. Both types of

liposomes resulted in a significant improvement in the circulation time of BSH compared to that obtained previously after injecting free BSH. The mean percent injected BSH remaining in circulation at the end of 24 h was 19% for the PEG-liposomes compared to the corresponding value of 7% for the conventional liposomes. The mean percent uptake by the liver and spleen was not significantly different for the 2 types of liposomes; the blood/RES ratios were higher for the PEG-liposomes at all time points indicating that a higher fraction of injected BSH was available in circulation. The PEG-liposomes could be further explored as a means of enhance boron drug delivery to tumor cells for BNCT.

SUPPL. TERM: liposome mercaptoundecahydrododecaborate boron neutron capture therapy

INDEX TERM: Blood
Liver
Reticuloendothelial system
Spleen
(liposomes containing mercaptoundecahydrododecaborate for boron neutron capture therapy)

INDEX TERM: **Radiotherapy**
(boron-neutron capture, liposomes containing mercaptoundecahydrododecaborate for boron neutron capture therapy)

INDEX TERM: **Pharmaceutical** dosage forms
(liposomes, liposomes containing mercaptoundecahydrododecaborate for boron neutron capture therapy)

INDEX TERM: 144885-51-8, Sodium mercaptoundecahydrododecaborate
ROLE: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(liposomes containing mercaptoundecahydrododecaborate for boron neutron capture therapy)

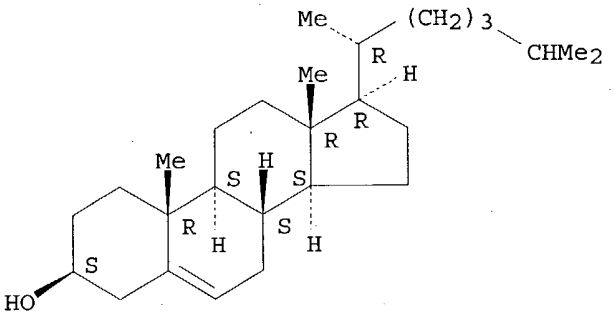
INDEX TERM: **57-88-5**, CHOLesterol, biological studies
2644-64-6, DPPC **5681-36-7D**,
Dipalmitoylphosphatidylethanolamine, reaction products with PEG 25322-68-3D, PEG, reaction products with DPPE
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing mercaptoundecahydrododecaborate for **boron** neutron capture therapy)

IT **57-88-5**, CHOLesterol, biological studies **2644-64-6**, DPPC **5681-36-7D**, Dipalmitoylphosphatidylethanolamine, reaction products with PEG
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes containing mercaptoundecahydrododecaborate for **boron** neutron capture therapy)

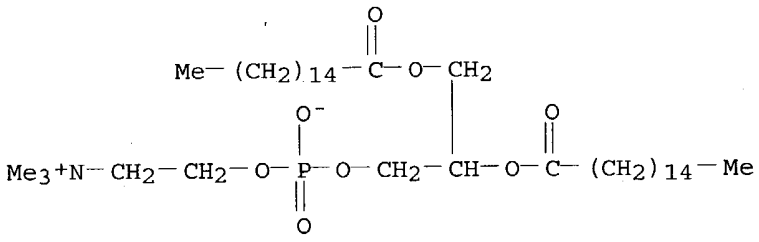
RN 57-88-5 HCAPLUS

CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

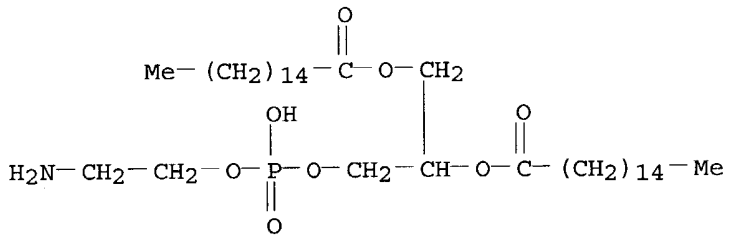
Absolute stereochemistry.



RN 2644-64-6 HCAPLUS
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



RN 5681-36-7 HCAPLUS
CN Hexadecanoic acid, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester (9CI) (CA INDEX NAME)



L131 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:423728 HCAPLUS
DOCUMENT NUMBER: 125:123458
ENTRY DATE: Entered STN: 18 Jul 1996
TITLE: Characterization of liposomal systems entrapping boron-containing compounds in response to pH gradients
AUTHOR(S): Moraes, Angela M.; Santana, Maria Helena A.; Carbonell, Ruben G.
CORPORATE SOURCE: Dept. Proc. Quimicos, State University Campinas, Campinas, 13083-000, Brazil
SOURCE: Biofunctional Membranes, [Proceedings of the International Conference on Biofunctional Membranes], Lexington, Ky., Apr. 9-11, 1995 (**1996**),

Meeting Date 1995, 259-275. Editor(s): Butterfield, D. Allan. Plenum: New York, N. Y.
CODEN: 63AXAU
DOCUMENT TYPE: Conference
LANGUAGE: English
CLASSIFICATION: 63-5 (Pharmaceuticals)
Section cross-reference(s): 8

ABSTRACT:
Boron neutron capture therapy (BNCT) is based on the nuclear reaction that occurs when a stable isotope, boron-10, is irradiated with low-energy thermal neutrons to yield ionizing helium and lithium ions that are highly damaging and usually lethal to cells. The successful treatment of cancer by BNCT requires the selective concentration of boron-10 within malignant tumors. Liposomes have been
used as drug delivery vehicles for in vivo application, including several anticancer agents. The ability of two boron-containing compds., l-p-borono-phenylalanine (BPA) HCl and o-carboranylpropylamine chloride (CPA) to accumulate within **unilamellar** liposomes passively and in response to a transmembrane pH gradient are compared. Characterization of the obtained systems is performed for conventional and polyethylene glycol (PEG)-modified (stealth) liposomes, in terms of lipid and drug contents, vesicle size and stability. The results indicate that BPA can be successfully encapsulated in conventional liposomes by passive loading, while the active loading approach is more suitable for the entrapment of CPA.

SUPPL. TERM: boron compd liposome encapsulation pH; neutron capture radiotherapy liposome boron compd

INDEX TERM: Encapsulation
Neoplasm
Particle size
(liposomes encapsulation of boron-containing compds. in response to pH gradients for neutron capture therapy)

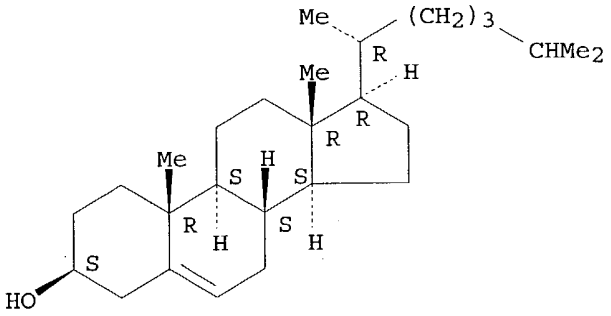
INDEX TERM: Pharmaceutical dosage forms
(liposomes, liposomes encapsulation of boron-containing compds. in response to pH gradients for neutron capture therapy)

INDEX TERM: Radiotherapy
(neutron capture, liposomes encapsulation of boron-containing compds. in response to pH gradients for neutron capture therapy)

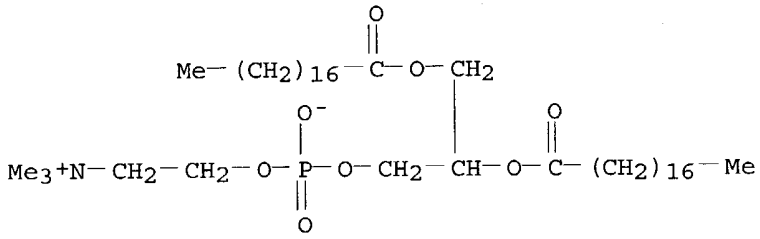
INDEX TERM: **57-88-5**, Cholesterol, biological studies
4539-70-2, Distearoyl phosphatidylcholine
7440-42-8D, Boron, compds. 20255-95-2, Dimyristoyl phosphatidylethanolamine 76410-59-8 140662-87-9 179484-10-7
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes encapsulation of **boron**-containing compds. in response to pH gradients for neutron capture therapy)

IT **57-88-5**, Cholesterol, biological studies **4539-70-2**, Distearoyl phosphatidylcholine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposomes encapsulation of **boron**-containing compds. in response to pH gradients for neutron capture therapy)
RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 4539-70-2 HCAPLUS
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)



L131 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:3825 HCAPLUS
DOCUMENT NUMBER: 120:3825
ENTRY DATE: Entered STN: 08 Jan 1994
TITLE: Use of fluorescent cholesteryl ester **microemulsions** in cholesteryl ester transfer protein assays
AUTHOR(S): Bisgaier, Charles L.; Minton, Laura L.; Essenburg, Arnold D.; White, Andrew; Homan, Reynold
CORPORATE SOURCE: Dep. Pharmacol., Parke-Davis Pharm. Res., Ann Arbor, MI, 48105, USA
SOURCE: Journal of Lipid Research (**1993**), 34(9), 1625-34
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 9-5 (Biochemical Methods)
ABSTRACT:
In the present report the authors describe a simple and practical method to assess CETP activity in a defined system by use of **microemulsions** containing a fluorescent cholesteryl ester analog. The **microemulsions** are stable, simple to prepare, and can be made to defined composition Initial transfer rates are easily determined by monitoring changes in fluorescence. The authors have used the fluorescent cholesteryl ester analog, cholesteryl 4,4-difluoro-5,7-dimethyl-4-bora-3α,4α-diaza-3-indacenedodecanoate (BODIPY-CE), to demonstrate the utility of this assay. The assay takes advantage of the concentration-dependent self-quenching of BODIPY-CE, when this analog
is incorporated into **microemulsions.** The authors have used this new assay to demonstrate fluorescent **lipid** transfer facilitated by rabbit

and human d>1.21 g/mL plasma fraction and recombinant human CETP. A known inhibitory monoclonal antibody (Mab) to human CETP blocked PODIPY-CE transfer in a dose-dependent manner. The authors have also used BODIPY-CE ***microemulsions*** to measure CETP activity in whole plasma.

SUPPL. TERM: cholesteryl ester transfer protein detn fluorometry; CETP protein **microemulsion** cholesterol ester fluorometry

INDEX TERM: Blood analysis
(cholesteryl ester transfer protein determination in human and laboratory animal, with **microemulsions** containing fluorescent cholesteryl ester)

INDEX TERM: **Lipids**, uses
ROLE: USES (Uses)
(**microemulsions**, for cholesteryl ester transfer protein determination, cholesteryl ester fluorescent analogs in)

INDEX TERM: Proteins, specific or class
ROLE: ANT (Analyte); ANST (Analytical study)
(cholesterol ester-exchanging, determination of, of human and laboratory animal plasma, fluorescent cholesteryl ester **microemulsions** in)

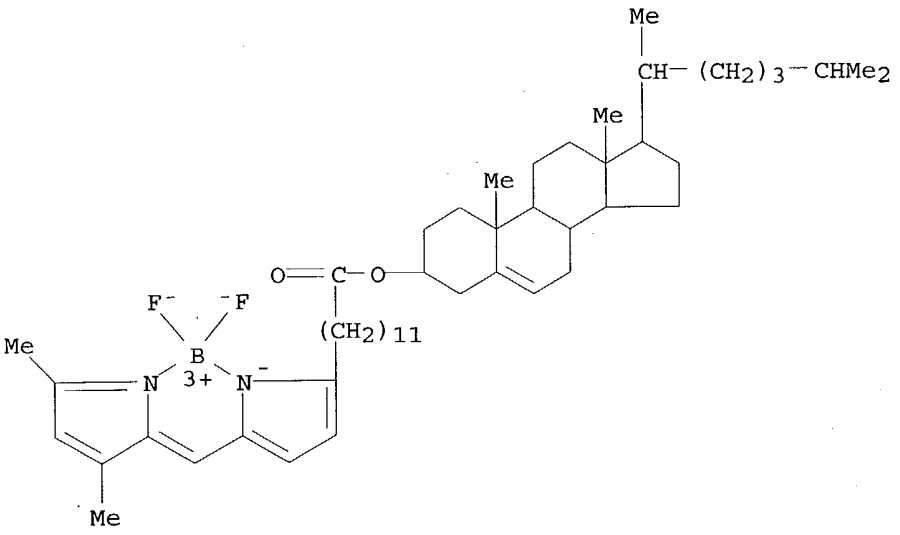
INDEX TERM: **Emulsions**
(micro-, **lipid**, cholesterol ester fluorescent analogs in, for cholesteryl ester transfer protein determination)

INDEX TERM: 57-88-5D, Cholesterol, esters, fluorescent
151736-99-1
ROLE: ANST (Analytical study)
(in cholesteryl ester transfer protein determination of plasma, in **microemulsions**)

IT **151736-99-1**
RL: ANST (Analytical study)
(in cholesteryl ester transfer protein determination of plasma, in **microemulsions**)

RN 151736-99-1 HCAPLUS

CN Boron, [(3β)-cholest-5-en-3-yl 5-[(3,5-dimethyl-2H-pyrrol-2-ylidene)methyl]-1H-pyrrole-2-dodecanoato-κN1,κN5]difluoro-, (T-4)- (9CI) (CA INDEX NAME)



L131 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:37930 HCAPLUS
DOCUMENT NUMBER: 120:37930
ENTRY DATE: Entered STN: 22 Jan 1994
TITLE: Characterization of biotinylated **liposomes** for in vivo targeting applications
AUTHOR(S): Loughrey, Helen C.; Ferraretto, Anita; Cannon, Ann-Marie; Acerbis, Giulia; Sudati, Francesco; Bottiroli, Giovanni; Masserini, Massimo; Soria, Marco R.
CORPORATE SOURCE: Department of Biochemistry, University College Galway, Galway, Ire.
SOURCE: FEBS Letters (**1993**), 332(1-2), 183-8
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 63-5 (Pharmaceuticals)
Section cross-reference(s): 1

ABSTRACT:
Liposomes containing monosialoganglioside (GM1) or polyethylene glycol (PEG) **lipid** derivs. have prolonged circulation in the blood. This favors **liposome** extravasation to tumor sites. In this report it is shown that inclusion of GM1, PEG550-DPPE or PEG2000-DPPE in **liposomes** containing biotin-DPPE significantly diminished the ability of vesicles to bind to ***streptavidin*** in vitro. Steric inhibition due to the bulky head group of these **lipids** was least for biotin-DPPE **liposomes** containing GM1. Biodistribution studies in C26 tumor-bearing mice showed that GM1-***liposomes*** containing small amts. of biotin-DPPE have long circulation life-times in the blood. Using fluorescent microscopic techniques, ***liposomes*** containing both GM1 and biotin-DPPE were detected within extra-vascular spaces in tumors. In addition it was shown that biotin-DPPE in GM1-**liposomes** bound **streptavidin** in situ. These results suggest that GM1-**liposomes** containing biotin-DPPE have potential use as diagnostic or therapeutic reagents in pre-targeting applications dependent on the high-affinity interaction of biotin with **streptavidin.**

SUPPL. TERM: biotinylated **liposome streptavidin**

binding tumor targeting; monosialoganglioside GM1 biotinylated **liposome streptavidin** tumor

INDEX TERM: Neoplasm
(biotinylated **liposomes** targeting to, **streptavidin** binding in relation to)

INDEX TERM: **Phosphatidylcholines, biological studies**
ROLE: BIOL (Biological study)
(egg yolk, biotinylated **liposomes** containing, **streptavidin** binding to, tumor targeting in relation to)

INDEX TERM: Pharmaceutical dosage forms
(**liposomes**, large **unilamellar**, biotinylated, **streptavidin** binding to, tumor targeting in relation to)

INDEX TERM: 9013-20-1, **Streptavidin**???
ROLE: PROC (Process)
(binding of, to biotinylated **liposomes**, tumor targeting in relation to)

INDEX TERM: 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
37758-47-7, Ganglioside GM1 **151911-45-4**
ROLE: BIOL (Biological study)
(biotinylated **liposomes** containing, **streptavidin** binding to, tumor targeting in relation to)

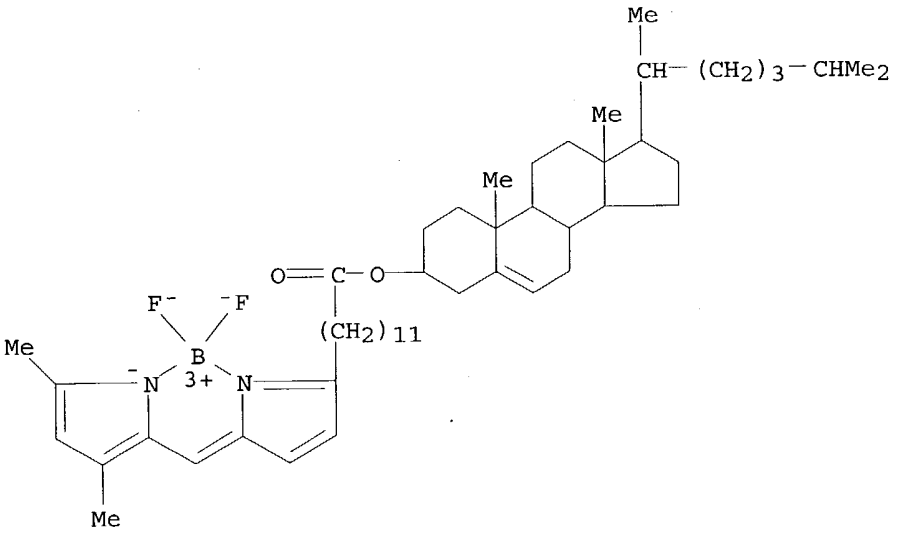
INDEX TERM: 116643-36-8 151835-78-8
ROLE: BIOL (Biological study)
(**liposomes** containing, **streptavidin** binding to, tumor targeting in relation to)

IT **37758-47-7**, Ganglioside GM1 **151911-45-4**
RL: BIOL (Biological study)
(biotinylated **liposomes** containing, **streptavidin** binding to, tumor targeting in relation to)

RN 37758-47-7 HCAPLUS
CN Ganglioside GM1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 151911-45-4 HCAPLUS
CN Boron, [(3β)-cholest-5-en-3-yl 2-[(3,5-dimethyl-1H-pyrrol-2-yl-κN)methylene]-2H-pyrrole-5-dodecanoato-κN1]difluoro-, (T-4)-(9CI) (CA INDEX NAME)



L131 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:213162 HCAPLUS
DOCUMENT NUMBER: 112:213162
ENTRY DATE: Entered STN: 09 Jun 1990
TITLE: Application of boronated anti CEA-immunoliposome to boron neutron capture therapy
AUTHOR(S): Yanagie, Hironobu; Fujii, Yuzo; Takahashi, Tsukasa; Sekiguchi, Morimasa; Uchida, Hisanori; Nariuchi, Hideo; Tomita, Toshio; Yasuda, Tatuji; Kobayashi, Hisao; et al.
CORPORATE SOURCE: Inst. Med. Sci., Univ. Tokyo, Tokyo, 108, Japan
SOURCE: Kyoto Daigaku Genshiro Jikkensho Gakujutsu Koenkai Koen Yoshishu (**1990**), 24, 71-7
CODEN: KDGYDY; ISSN: 0287-9131
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
CLASSIFICATION: 8-9 (Radiation Biochemistry)
Section cross-reference(s): 14, 63

ABSTRACT:
A selective drug delivery system for B-neutron capture therapy (BNCT) of noncerebral tumors was established, consisting of anti-CEA monoclonal antibody (4 mg/mL) conjugated with liposomes which contained 10B-compound (623 ppm) inside. The immunoliposomes attached to CEA-producing human pancreatic carcinoma cells, AsPC-1, and suppressed the cell growth in vitro upon thermal neutron irradiation (1 + 1012 neutrons/cm2 flux). The suppression was dependent on the concentration of 10B-compound within liposomes and the d. of antibody
conjugated to liposome. These results suggested that immunoliposomes containing 10B-compound could provide a selective and efficient carrier of B atoms to target tumor cells for BNCT.

SUPPL. TERM: boron neutron capture radiotherapy tumor; antibody liposome boron neutron capture therapy
INDEX TERM: Neoplasm, toxic chemical and physical damage
(boron compound-containing immunoliposomes damage to, in boron-neutron capture radiotherapy)
INDEX TERM: Neoplasm inhibitors

(boron compound-containing immunoliposomes, in boron-neutron capture radiotherapy)

INDEX TERM: **Phosphatidylcholines, biological studies**
ROLE: BIOL (Biological study)
(immunoliposomes containing, for boron-neutron capture radiotherapy of tumors)

INDEX TERM: Antigens
ROLE: BIOL (Biological study)
(CEA (carcinoembryonic antigen), monoclonal antibodies to, in boronated liposomes for boron-neutron capture radiotherapy of tumors)

INDEX TERM: Pancreas, neoplasm
(carcinoma, boron compound-containing immunoliposomes damage to, in boron-neutron capture radiotherapy)

INDEX TERM: **Radiotherapy**
(immuno-, boron-neutron capture, of tumors, with boron compound-containing immunoliposomes)

INDEX TERM: **Pharmaceutical** dosage forms
(liposomes, containing monoclonal antibodies, for boron-neutron capture radiotherapy of tumors)

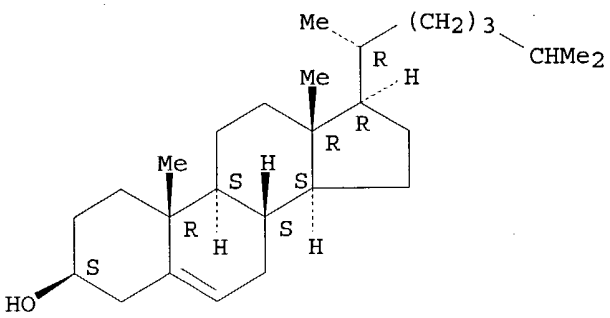
INDEX TERM: Antibodies
ROLE: BIOL (Biological study)
(monoclonal, against carcinoembryonic antigen, in liposomes containing boron compds., for boron-neutron capture radiotherapy of tumors)

INDEX TERM: **57-88-5**, Cholesterol, biological studies
109742-44-1 126938-07-6
ROLE: BIOL (Biological study)
(immunoliposomes containing, for **boron**-neutron capture radiotherapy of tumors)

INDEX TERM: 12586-31-1
ROLE: BIOL (Biological study)
(radiotherapy, immuno-, boron-neutron capture, of tumors, with boron compound-containing immunoliposomes)

IT **57-88-5**, Cholesterol, biological studies
RL: BIOL (Biological study)
(immunoliposomes containing, for **boron**-neutron capture radiotherapy of tumors)
RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d l131 ibib ab 17-25
YOU HAVE REQUESTED DATA FROM FILE 'USPATFULL, HCAPLUS, BIOSIS' - CONTINUE? (Y)/N:y

L131 ANSWER 17 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
ACCESSION NUMBER: 2002:348359 BIOSIS
DOCUMENT NUMBER: PREV200200348359
TITLE: **Carborane** containing **cholesterol**, a new type of molecule for targeted **boron drug delivery.**
AUTHOR(S): Lu, Donghao Robert [Inventor, Reprint author]; Ji, Bing Qing [Inventor]
CORPORATE SOURCE: Athens, GA, USA
ASSIGNEE: The University of Georgia Research Foundation, Inc., Athens, GA, USA
PATENT INFORMATION: US 6392068 May 21, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (May 21, 2002) Vol. 1258, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jun 2002
Last Updated on STN: 19 Jun 2002
AB The present invention relates to novel **carborane cholesterol** analogs and their use in the treatment of tumor and cancers in humans, and in particular to the treatment of human brain tumors. **Pharmaceutical** compositions and methods of using these compositions in the treatment of tumors and cancer are other aspects of the present invention.

L131 ANSWER 18 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2004:172437 BIOSIS
DOCUMENT NUMBER: PREV200400173455
TITLE: In vitro uptake of a new **cholesteryl carborane** ester compound by human glioma cell lines.
AUTHOR(S): Peacock, Gina; Sidwell, Richard; Pan, Guangliang; Oie, Svein; Lu, D. Robert [Reprint Author]
CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of Pharmacy, Temple University, 3307 North Broad Street, Philadelphia, PA, 19140, USA
rlu@temple.edu
SOURCE: Journal of Pharmaceutical Sciences, (January 2004) Vol. 93, No. 1, pp. 13-19. print. CODEN: JPMSAE. ISSN: 0022-3549.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Mar 2004
Last Updated on STN: 31 Mar 2004
AB The cellular uptake and retention of a new **cholesteryl carborane** ester compound, **cholesteryl** 1,12-dicarba-closo-**dodecaboranel**-carboxylate (BCH), by two human glioma cell lines, glioblastoma multiforme SF-763 and SF-767, was evaluated. BCH, which is an extremely **hydrophobic** compound, was formulated into liposomes and incubated with two human glioma tumor cell lines and one human normal neuron cell line. The amount of BCH uptake by the cells was measured by high performance liquid chromatography. The effects of BCH concentration in the culture medium and the incubation time on the cellular uptake of BCH were studied. In addition, BCH uptake by

tumor cells was examined in the presence and absence of lipoprotein in the culture medium. It was found that the amount of BCH taken by the glioma cell lines was much more (up to 14 times) than that by the normal neuron cell line. The cellular uptake of BCH was related to the amount of BCH in the medium as well as the incubation time. The cellular uptake of BCH by SF-763 and SF-767 cells after 16 h of incubation was 283.3+-38.9 and 264.0+-36.5 mug **boron**/g cells, respectively. The majority of BCH taken up in tumor cells was retained after the subsequent incubation. In the presence of lipoprotein, the cellular uptake of BCH by SF-767 tumor cells was about four times as much as that in the absence of lipoprotein. In conclusion, the cellular uptake of BCH by glioma cells was about 14 times higher than by normal neuron cells. The uptake in glioma cells was up to 10 times higher than that required for successful cancer treatment and BCH was well retained in the tumor cells. Lipoprotein seemed to have an important role in the BCH uptake by glioma cells.

L131 ANSWER 19 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:274501 BIOSIS
DOCUMENT NUMBER: PREV200300274501
TITLE: Synthesis, preformulation and liposomal formulation of **cholesteryl carborane** esters with various fatty chains.
AUTHOR(S): Alanazi, Fars; Li, Hengguang; Halpern, David S.; Oie, Svein; Lu, D. Robert [Reprint Author]
CORPORATE SOURCE: Department of Pharmaceutical and Biomedical Science, College of Pharmacy, University of Georgia, Athens, GA, 30602, USA
rlu@rx.uga.edu
SOURCE: International Journal of Pharmaceutics (Kidlington), (14 April 2003) Vol. 255, No. 1-2, pp. 189-197. print.
ISSN: 0378-5173 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003

AB The elevated expression of LDL receptor on tumor cells provides one attractive approach for targeted drug delivery to tumor cells. Suitable antitumor compounds, however, need to be synthesized and developed which mimic the native **cholesteryl** esters (as major constituent of LDL) in chemical structure for targeted delivery to tumor cells through the over-expressed LDL receptors. In the present study, new antitumor compounds were designed containing **cholesterol**, fatty chain and **carborane** which is used as the antitumor unit. Three new compounds were synthesized with a three-step reaction scheme. Similar to the native **cholesteryl** esters, these compounds are extremely **hydrophobic** and, before any further biological studies, suitable liposomal formulations for these new compounds are required. Various liposomal formulations as well as the preformulation characterization of these new compounds were thus examined. The incorporation efficiency of the compounds in liposomes was found to vary significantly depending on the type of fatty chain attached and the ratio of **cholesterol** :phospholipid used as the excipients of liposomal formulation.

L131 ANSWER 20 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:411356 BIOSIS
DOCUMENT NUMBER: PREV200300411356
TITLE: Liposomes from novel carborane-containing lipids for **boron neutron capture** therapy.
AUTHOR(S): Li, Tiejun [Reprint Author]; Thomas, Jason [Reprint Author]; Hawthorne, M. Frederick [Reprint Author]

CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of California, 405 Hilgard Avenue, Los Angeles, CA, 90095-1569, USA
tli@chem.ucla.edu
SOURCE: Abstracts of Papers American Chemical Society, (2003) Vol. 225, No. 1-2, pp. INOR 161. print.
Meeting Info.: 225th American Chemical Society (ACS) National Meeting. New Orleans, LA, USA. March 23-27, 2003. American Chemical Society.
ISSN: 0065-7727 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Sep 2003
Last Updated on STN: 10 Sep 2003

L131 ANSWER 21 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:505479 BIOSIS
DOCUMENT NUMBER: PREV200200505479
TITLE: Synthesis of **cholesterol-carborane** conjugate for targeted **drug delivery.**
AUTHOR(S): Ji, Bingqing; Peacock, Gina; Lu, D. Robert [Reprint author]
CORPORATE SOURCE: Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, University of Georgia, Athens, GA, 30602, USA
rlu@rx.uga.edu
SOURCE: Bioorganic and Medicinal Chemistry Letters, (September, 2002) Vol. 12, No. 17, pp. 2455-2458. print.
CODEN: BMCLE8. ISSN: 0960-894X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002
AB The **cholesterol-carborane** conjugate has been designed and synthesized to selectively deliver **boron** to tumor cells by means of reconstituted low-density lipoprotein. The chemical stability and cytotoxicity of the new compound have been examined. Several methods have been evaluated for incorporation of the compound into LDL.

L131 ANSWER 22 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:384246 BIOSIS
DOCUMENT NUMBER: PREV200200384246
TITLE: **VLDL**-resembling phospholipid-submicron **emulsion** for cholesterol-based drug targeting.
AUTHOR(S): Shawer, Mohannad; Greenspan, Phillip; Oie, Svein; Lu, D. Robert [Reprint author]
CORPORATE SOURCE: Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, University of Georgia, Athens, GA, 30602, USA
rlu@rx.uga.edu
SOURCE: Journal of Pharmaceutical Sciences, (June, 2002) Vol. 91, No. 6, pp. 1405-1413. print.
CODEN: JPMSAE. ISSN: 0022-3549.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jul 2002
Last Updated on STN: 10 Jul 2002
AB The objective of the current study was to develop and evaluate VLDL-resembling phospholipid-submicron **emulsion** (PSME) as a carrier system for new **cholesterol**-based compounds for targeted

delivery to cancer cells. BCH, a **boronated cholesterol** compound, was originally developed in our laboratory to mimic the **cholesterol** esters present in the LDL and to follow a similar pathway of **cholesterol** transport into the rapidly dividing cancer cells. The VLDL-resembling system was then designed to solubilize BCH, facilitate the interaction with LDL, and thus assist the BCH delivery to cancer cells. BCH-containing PSME was prepared by sonication. Chemical compositions and particle sizes of different PSME fractions were determined. The lipid structure of PSME and location of BCH in the formulation were assessed based on experimental results. Density gradient ultracentrifugation fractionated the **emulsion** into three particle-size populations with structures and compositions resembling native VLDL. In vitro interaction between PSME, and LDL was evident by agarose electrophoresis, as both formed a single band with an intermediate mobility. The transfer of BCH from PSME to LDL was also observed in the presence of other serum components including serum proteins. Cell culture data showed sufficient uptake of BCH in rat 9L glioma cells (>50 mug **boron**/g cells). In conclusion, this system has the capability to incorporate the **cholesterol**-based compound, interact with native LDL, and assist the delivery of this compound into cancer cells in vitro.

L131 ANSWER 23 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1997:30890 BIOSIS
DOCUMENT NUMBER: PREV199799337293
TITLE: Selective uptake of boronated low-density lipoprotein in melanoma **xenografts** achieved by diet supplementation.
AUTHOR(S): Setiawan, Y.; Moore, D. E. [Reprint author]; Allen, B. J.
CORPORATE SOURCE: Dep. Pharmacy, University Sydney, Sydney, NSW 2006, Australia
SOURCE: British Journal of Cancer, (1996) Vol. 74, No. 11, pp. 1705-1708.
CODEN: BJCAAI. ISSN: 0007-0920.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
AB The lipid **core** of human plasma low-density lipoprotein (LDL) was extracted using hexane and the LDL reconstituted with the addition of n-octyl-**carborane**. Biodistribution studies of the **boronated** LDL were performed in BALB/c mice bearing subcutaneous Harding-Passey melanoma xenografts. When diet supplementation with coconut oil and **cholesterol** for 21 days and regular dosing with hydrocortisone for 7 days before the studies was used to down-regulate the liver LDL receptors and the adrenal receptors, respectively, the tumour-blood **boron** concentration ratio of 5:1 was achieved.

L131 ANSWER 24 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:209048 BIOSIS
DOCUMENT NUMBER: PREV199598223348
TITLE: Selective boron delivery to **murine tumors** by lipophilic species incorporated in the membranes of **unilamellar** liposomes.
AUTHOR(S): Feakes, Debra A.; Shelly, Kenneth; Hawthorne, M. Frederick [Reprint author]
CORPORATE SOURCE: Dep. Chem. Biochem., Univ. California Los Angeles, Los Angeles, CA 90024, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 5, pp. 1367-1370.

CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 May 1995
Last Updated on STN: 23 May 1995

AB The nido-**carborane** species K(nido-7-CH-3(CH-2)-15-7,8-C-2B-9H-11) has been synthesized for use as an addend for the **bilayer** membrane of liposomes. Small **unilamellar** vesicles, composed of distearoylphosphatidylcholine/**cholesterol**, 1:1, and incorporating K(nido-7-CH-3(CH-2)-15-7,8-C-2B-9H-11) in the **bilayer**, have been investigated in vivo. The time-course biodistribution of **boron** delivered by these liposomes was determined by inductively coupled plasma-atomic emission spectroscopy analyses after the injection of liposomal suspensions in BALB/c mice bearing EMT6 mammary adenocarcinomas. At the low injected doses normally used (apprxeq 5-10 mg of **boron** per kg of body weight), peak tumor **boron** concentrations of apprxeq 35 mu-g of **boron** per g of tissue and tumor/blood **boron** ratios of apprxeq 8 were achieved. These values are sufficiently high for the successful application of **boron** neutron capture therapy. The **bilayer**-embedded **boron** compound may provide the sole **boron** source or, alternatively, a concentrated aqueous solution of a **hydrophilic boron** compound may also be encapsulated within the liposomes to provide a dose enhancement. Thus, the incorporation of both K(nido-7-CH-3(CH-2)-15-7,8-C-2B-9H-11) and the **hydrophilic** species, Na-3(1-(2'-B-10H-9)-2-NH-3B-10H-8), within the same liposomes demonstrated significantly enhanced biodistribution characteristics, exemplified by maximum tumor **boron** concentrations of apprxeq 50 mu-g of **boron** per g of tissue and tumor/blood **boron** ratios of apprxeq 6.

L131 ANSWER 25 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:6640 BIOSIS
DOCUMENT NUMBER: PREV199395006640
TITLE: Model studies directed toward the **boron neutron-capture** therapy of cancer: Boron delivery to **murine tumors** with liposomes.
AUTHOR(S): Shelly, Kenneth; Feakes, D. A.; Hawthorne, M. Frederick [Reprint author]; Schmidt, Paul G.; Krisch, Teresa A.; Bauer, William F.
CORPORATE SOURCE: Dep. Chemistry Biochemistry, University California, Los Angeles, Calif. 90024, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1992) Vol. 89, No. 19, pp. 9039-9043.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1992
Last Updated on STN: 13 Dec 1992

AB The successful treatment of cancer by **boron** neutron-capture therapy (BNCT) requries the selective concentration of **boron**-10 within malignant tumors. The potential of liposomes to deliver **boron**-rich compounds to tumors has been assessed by the examination of the biodistribution of **boron** delivered by liposomes in tumor-bearing mice. Small **unilamellar** vesicles with mean diameters of 70 mm or less, composed of a pure synthetic phospholipid (distearoyl phosphatidylcholine) and **cholesterol**, have been found to stably encapsulate high concentrations of water-soluble

ionic **boron** compounds. The hydrolytically stable **borane** anions B-10H-10-2-, B-12H-11SH-2- B-20H-17OH-4-, B-20H1-9-3-, and the normal form and photoisomer of B-20H-18-2- were encapsulated in liposomes as their soluble sodium salts. The tissue concentration of **boron** in tumor-bearing mice was measured at several time points over 48 h after i.v. injection of **emulsions** of liposomes containing the **borane** anions. Although the **boron** compounds used do not exhibited an affinity for tumors and are normally rapidly cleared from the body, liposomes were observed to selectively deliver the **borane** anions to tumors. The highest tumor concentrations achieved reached the therapeutic range (gt 15 mu-g of **boron** per g of tumor) while maintaining high tumor-**boron**/blood-**boron** ratios (gt 3). The most favorable results were obtained with the two isomers of B-20H-18-2-. These **boron** compounds have the capability to react with intracellular components after they have been deposited within tumor cells by the liposome, thereby preventing the **borane** ion from being released into blood.

=> d l131 ibib ab kwic 26
YOU HAVE REQUESTED DATA FROM FILE 'USPATFULL, HCAPLUS, BIOSIS' - CONTINUE? (Y)/N:y

L131 ANSWER 26 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2000:127960 USPATFULL
TITLE: Optoacoustic contrast agents and methods for their use
INVENTOR(S): Unger, Evan C., Tucson, AZ, United States
Wu, Yunqiu, Tucson, AZ, United States
PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., Tucson, AZ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6123923		20000926	
APPLICATION INFO.:	US 1997-993165		19971218	(8)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1997-46379P	19970513	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose' G.
ASSISTANT EXAMINER: Sharareh, Shahnam
LEGAL REPRESENTATIVE: Woodcock Washburn Kurtz Mackiewcz & Norris LLP
NUMBER OF CLAIMS: 54
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 6923
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention generally relates to optoacoustic contrast agents and methods of diagnostic and therapeutic imaging using optoacoustic contrast agents.

DRWD FIG. 4 is an embodiment of a composition of the present invention where photoactive agents are incorporated in an oily **hydrophobic** mantle (1) in the vesicles, and where a gas phase (2) is incorporated in the interior of the vesicle.

DETD "Lipid" refers to a naturally-occurring, synthetic or semi-synthetic (i.e., modified natural) compound which is generally **amphipathic** . The lipids typically comprise a **hydrophilic** component and a

hydrophobic component. Suitable lipids include, for example, fatty acids, neutral fats, fluorinated lipids, phosphatides, oils, fluorinated oils, glycolipids, surface active agents. . .

DETD . . . a compound that alters surface tension. Surface active agents include, for example, detergents, wetting agents, dispersing agents, foaming agents and **emulsifiers.** Preferable examples of surfactants are **hydrophobic** compounds, including phospholipids, oils, fluorinated oils and fluorosurfactants.

DETD "Amphiphilic moiety" or "amphiphile" refers to a synthetic, semi-synthetic (modified natural) or naturally-occurring compound having a water-soluble, **hydrophilic** portion and a water-insoluble, **hydrophobic** portion. Preferred amphiphilic compounds have a polar head group, for example, a phosphatidylcholine group, and one or more nonpolar, aliphatic. . . "Perfluorinated amphiphilic moiety" refers to amphiphilic compounds in which all the hydrogen atoms have been replaced with a fluorine atom. "**Amphipathy**" refers to the simultaneous attraction and repulsion in a single molecule or ion containing one or more groups having an affinity for the phase or medium in which they are dissolved, **emulsified** and/or suspended, together with one or more groups that tend to be expelled from the involved phase or medium.

DETD . . . walls or membranes may be concentric or otherwise. The stabilizing compounds may be in the form of one or more **monolayers** or **bilayers.** In the case of more than one **monolayer** or **bilayer**, the **monolayers** or **bilayers** may be concentric. Stabilizing compounds may be used to form a **unilamellar** vesicle (comprised of one **monolayer** or **bilayer**), an **oligolamellar** vesicle (comprised of about two or about three **monolayers** or **bilayers**) or a **multilamellar** vesicle (comprised of more than about three **monolayers** or **bilayers**). The walls or membranes of vesicles may be substantially solid (uniform), or they may be porous or semi-porous. The internal. . .

DETD "Liposome" refers to a generally spherical or spheroidal cluster or aggregate of **amphipathic** compounds, including lipid compounds, typically in the form of one or more concentric **layers**, for example, **bilayers.** They may also be referred to as lipid vesicles or lipid microspheres. The liposomes may be formulated, for example, from. . .

DETD "**Micelle**" refers to **colloidal** entities formulated from lipids. In preferred embodiments, **micelles** comprise a **monolayer**, **bilayer**, or hexagonal H II phase structure.

DETD "**Emulsion**" refers to a mixture of two or more generally immiscible liquids, and is generally in the form of a **colloid.** The mixture may be of lipids, for example, which may be homogeneously or heterogeneously dispersed throughout the **emulsion.**

DETD Alternatively, the lipids may be aggregated in the form of, for example, clusters or **layers**, including **monolayers** or **bilayers.**

DETD . . . phase structure" refers to a generally tubular aggregation of lipids in liquid media, for example, aqueous media, in which the **hydrophilic** portion(s) of the lipids generally face inwardly in association with an aqueous liquid environment inside the tube.

DETD The **hydrophobic** portion(s) of the lipids generally radiate outwardly and the complex assumes the shape of a hexagonal tube. A plurality of. . .

DETD . . . comprise a stabilizing material and a photoactive agent. "Optoacoustic contrast agent" also refers, for example, to delivery vehicles, vesicles, liposomes, **micelles**, **emulsions**, suspensions, dispersions, aerogels, clathrates, hexagonal H II phase

structures and the like. Such contrast agents are capable of providing an. . .

DETD . . . a photoactive agent, a bioactive agent and/or a targeting ligand. Suitable delivery vehicles include, for example, stabilizing materials, vesicles, liposomes, **micelles**, aerogels, clathrates, gas and/or gaseous precursor filled vesicles, **emulsions**, suspensions, dispersions, hexagonal H II phase structures, cochleates and the like.

DETD . . . containing the photoactive agents, gases, gaseous precursors, liquids, bioactive agents and/or targeting ligands described herein, including, for example, mixtures, suspensions, **emulsions**, dispersions, vesicles, or the like. The improved stability involves, for example, the maintenance of a relatively balanced condition, and may. . . maintained entrapped until release is desired. Exemplary stabilizing materials include lipids, proteins, polymers, carbohydrates and surfactants. The resulting mixture, suspension, **emulsion** or the like may comprise walls (e.g., films, membranes and the like) around the photoactive agent, targeting ligand, bioactive agent,. . .

DETD "**Hydrophilic** interaction" refers to molecules or portions of molecules which may substantially bind with, absorb and/or dissolve in water. This may. . .

DETD "**Hydrophobic** interaction" refers to molecules or portions of molecules which do not substantially bind with, absorb and/or dissolve in water. "Biocompatible". . .

DETD . . . refers to the incorporation of photoactive agents, bioactive agents and/or targeting ligands in stabilizing compositions of the present invention, including **emulsions**, suspensions, vesicles and the like. Photoactive agents, bioactive agents and/or targeting ligands can be combined with the stabilizing compositions in. . . within the internal void of the vesicles. Photoactive agents, bioactive agents and/or targeting ligands may also be integrated within the **layer**(s) or wall(s) of the vesicle, for example, by being interspersed among stabilizing materials which form or are contained within the vesicle **layer**(s) or wall(s). In addition, photoactive agents, bioactive agents and/or targeting ligands may be located on the surface of vesicles or. . . bioactive agents and/or targeting ligands may be concurrently entrapped within the internal void of the vesicle and/or integrated within the **layer**(s) or wall(s) of the vesicles and/or located on the surface of vesicles or non-vesicular stabilizing materials. Targeting ligands are preferably. . .

DETD . . . a vesicular membrane(s). Optically active contrast agents that are also highly acoustically active may be produced by incorporating lipophilic, preferably **amphipathic** photoactive agents into the lipid compositions.

DETD . . . example of an optoacoustic contrast agent of the present invention with an internal oil phase (1). A high concentration of **hydrophobic** photoactive agents (e.g., A-I) can be loaded into the interior of the oil phase within the vesicle by virtue of. . . an optoacoustic contrast agent with a higher concentration of photoactive agent than lipid-based compositions which may have only a thin **layer** (e.g., **monolayer** or **bilayer**) of lipid surrounding a gas phase. Depending upon the solubility of the photoactive agents in the oil phase, it is. . .

DETD . . . tissue specific targeting for the composition. The region for entrapment of photoactive agents (2) may be, for example, an oily **hydrophobic** region.

DETD . . . hydroxyl groups, such as triglycerides of d-12-hydroxyoleic acid, including castor oil and ergot oil. Polymerization may be designed to include **hydrophilic** substituents such as carboxyl or

hydroxyl groups, to enhance dispersability so that the backbone residue resulting from biodegradation is water. . .

DETD . . . surface tension on the vesicle membrane or skin. It is possible that propylene glycol can also function as an additional **layer** that may coat the membrane or skin of the vesicle, thus providing additional stabilization. The surfactants described in U.S. Pat.. . .

DETD Compounds used to make mixed **micelle** systems may be used as basic or auxiliary stabilizing materials, and include, for example, sodium dodecyl sulfate, cetylammonium halides, cetylalkylammonium. . .

DETD . . . of vesicles to rupture by fusing together. Thus, the negatively charged lipids may act to establish a uniform negatively charged **layer** on the outer surface of the vesicle, which will be repulsed by a similarly charged outer **layer** on other vesicles which are proximate thereto. In this way, the vesicles may be less prone to come into touching. . .

DETD . . . 2; X.sub.3 is a direct bond or --O--; M is P or S; Z is hydrogen, the residue of a **hydrophilic** polymer, a saccharide residue or --N(R.sub.6).sub.r, where r is 2 or 3; each R, is independently an alkyl group of. . . each R.sub.6 is independently hydrogen, an alkyl group of 1 to about 8 carbon atoms or a residue of a **hydrophilic** polymer; provided that at least one of x, y and z is 1, at least one of R.sub.1 is a. . .

DETD Z is hydrogen atom, the residue of a **hydrophilic** polymer, a saccharide residue or --N(R.sub.6).sub.r, where r is 2 or 3. In preferred embodiments, Z is --N(R.sub.6).sub.r.

DETD R.sub.6 is a hydrogen atom, an alkyl group of 1 to about 8 carbon atoms or a residue of a **hydrophilic** polymer. Preferably, R.sub.6 is a hydrogen atom or an alkyl group of 1 to about 4 carbon atoms. More preferably,. . .

DETD Z and R.sub.6 in the definition of Z in formula (IV), can be the residue of a **hydrophilic** polymer. Exemplary polymers from which Z and/or R.sub.6 can be derived include polymers in which the repeating units contain one. . .

DETD . . . 5,000 and PEG 8,000, which have molecular weights of 2,000, 5,000 and 8,000, respectively, being even more preferred. Other suitable **hydrophilic** polymers, in addition to those exemplified above, will be readily apparent to one skilled in the art based on the. . .

DETD In addition to residues of **hydrophilic** polymers, Z in formula (IV) can be a saccharide residue. Exemplary saccharides from which Z can be derived include, for. . .

DETD . . . disrupted vesicles. Fluorine can also be introduced into stabilizing materials and/or vesicles using other methods, such as sonication, spray-drying or **emulsification** techniques.

DETD . . . situated at the interface between the gas and the membrane or wall surface of the vesicle. Thus, an additional stabilizing **layer** of fluorinated liquid compound may be formed on the internal surface of the stabilizing composition which may also prevent any. . .

DETD . . . nonionic or zwitterionic lipid, (2) a negatively charged lipid, and (3) a lipid bearing a stabilizing material, for example, a **hydrophilic** polymer. Preferably, the amount of the negatively charged lipid will be greater than about 1 mole % of the total lipid present, and the amount of lipid bearing a **hydrophilic** polymer will be greater than about 1 mole % of the total lipid present. Exemplary and preferred negatively charged lipids include phosphatidic acids. The lipid bearing a **hydrophilic** polymer will desirably be a lipid covalently linked to the polymer, and the polymer will preferably have a weight average molecular weight of from about 400 to about 100,000. Suitable **hydrophilic** polymers are preferably selected from the group consisting of polyethylene glycol (PEG),

polypropylene glycol, polyvinyl alcohol, and polyvinyl pyrrolidone and. . . or other phospholipids, with a covalent bond including, for example, amide, ester, ether, thioester, thioamide or disulfide bonds. Where the **hydrophilic** polymer is PEG, a lipid bearing such a polymer will be said to be "pegylated." In preferred form, the lipid bearing a **hydrophilic** polymer may be DPPE-PEG, including, for example, DPPE-PEG5000, which refers to DPPE having a polyethylene glycol polymer of a mean. . .

DETD . . . and 100,000; and di- and trihydroxy alkanes and their polymers, preferably with molecular weight ranges between 200 and 50,000; (ii) **emulsifying** and/or solubilizing agents including, for example, acacia, cholesterol, diethanolamine, glyceryl monostearate, lanolin alcohols, lecithin, mono- and di-glycerides, mono-ethanolamine, oleic acid,. . . propylene glycol monostearate, sodium lauryl sulfate, sodium stearate, sorbitan mono-laurate, sorbitan mono-oleate, sorbitan mono-palmitate, sorbitan monostearate, stearic acid, trolamine, and **emulsifying** wax; (iii) suspending and/or viscosity-increasing agents, including, for example, acacia, agar, alginic acid, aluminum mono-stearate, bentonite, magma, carbomer 934P, carboxymethyl-cellulose,. . .

DETD . . . vesicles are desirably formulated in an aqueous environment which can induce the stabilizing material (e.g., a lipid because of its **hydrophobic-hydrophilic** nature) to form vesicles, which may be the most stable configuration which can be achieved in such an environment. The. . .

DETD . . . gaseous precursors may be incorporated, for example, in stabilizing materials in which the stabilizing materials are aggregated randomly, such as **emulsions**, dispersions or suspensions, as well as in vesicles, including vesicles such as cochleates, **micelles** and liposomes. Incorporation of the gases and/or gaseous precursors in the stabilizing materials and/or compositions may be achieved by a. . .

DETD . . . liquid to gaseous states at relatively close to normal body temperature (37° C.) or below, and the size of the **emulsified** droplets that would be required to form a vesicle of a maximum size of 10 μm.

DETD TABLE 1

Physical Characteristics of Gaseous Precursors and Diameter of **Emulsified** Droplet to Form a 10 μm Vesicle

Compound	Molecular Weight	Boiling Point (° C.)	Density	Diameter (μm) of **emulsified** droplet to make 10 μm vesicle
perfluoropentane	288.04	28.5	1.7326	2.9
1-fluorobutane	76.11	32.5.	.	.

DETD . . . be used as targeting ligands. Additionally, cholesterol may be used to target the endothelial cells and localize the stabilizing materials, **emulsions**, vesicles and the like, to regions of atherosclerotic plaque. In embodiments involving the use of cholesterol as a targeting ligand,. . .

DETD . . . or 2-azetidinone-4-carboxylic acid; B is serine, glycine, valine, alanine, threonine or β-alanine; C is an amino acid group having a **hydrophobic** functional group; and D is hydroxy or amino; wherein R.sub.1 is hydrogen, --(CH.sub.2).sub.p CH.sub.3 or --CO--(CH.sub.2).sub.p CH.sub.3 ; R.sub.2 is. . .

DETD where A is arotic acid or hydroorotic acid; B is an amino acid; C is an

amino acid having a **hydrophobic** functional group; and D is hydroxy or amino. In the above compounds, amino acids having **hydrophobic** functional groups in the definition of "C" include, for example, tryptophan and phenylalanine.

DETD . . . ligand is preferably covalently bound to the surface of the stabilizing material or vesicle by a spacer including, for example, **hydrophilic** polymers, such as the **hydrophilic** polymers described herein, preferably polyethylene glycol. Preferred molecular weights of the polymers are from 1000 da to 10,000 da, with. . .

DETD . . . be apparent to one skilled in the art in view of the present disclosure. Preferably, the linking group comprises a **hydrophilic** polymer. Suitable **hydrophilic** polymers include, for example, polyalkyleneoxides such as, for example, polyethylene glycol (PEG) and polypropylene glycol (PPG), polyvinylpyrrolidones, polyvinylmethylethers, polyacryl-amides, such. . . polyhydroxypropyl methacrylates, polymethyl-oxazolines, polyethyloxazolines, polyhydroxyethyl-oxazolines, polyhyhydroxypropyl-oxazolines, polyvinyl alcohols, polyphosphazenes, poly(hydroxyalkylcarboxylic acids), polyoxazolidines, polyaspartamide, and polymers of sialic acid (polysialics). The **hydrophilic** polymers are preferably selected from the group consisting of PEG, PPG, polyvinylalcohol and polyvinylpyrrolidone and copolymers thereof, with PEG and. . .

DETD . . . ligand. Thus, using the example DPPE-PEG, such as, for example, DPPE-PEG5000, the aforementioned conjugate may be represented as DPPE-PEG5000-TL. The **hydrophilic** polymer used as a linking group is preferably a bifunctional polymer, for example, bifunctional PEG, such as diamino-PEG. In this. . . to a lipid compound, and is bound at the free end to the targeting ligand via an amide linkage. A **hydrophilic** polymer, for example, PEG, substituted with a terminal carboxylate group on one end and a terminal amino group on the other end, may also be used. These latter bifunctional **hydrophilic** polymer may be preferred since they possess various similarities to amino acids.

DETD . . . used to link the targeting ligand to the lipid when utilizing linker groups having two unique terminal functional groups. Bifunctional **hydrophilic** polymers, and especially bifunctional PEGs, may be synthesized using standard organic synthetic methodologies. In addition, many of these materials are. . .

DETD . . . for example, hydroxy, thio and amine groups, which can react with a carboxylic acid or carboxylic acid derivative of the **hydrophilic** polymeric linker using suitable coupling conditions which would be apparent to one of ordinary skill in the art in view. . .

DETD . . . on a backbone of a polymer which is included in the vesicles, may be coupled to amine groups on a **hydrophilic** linking polymer by forming a Schiff's base, for example, by using coupling agents, such as glutaraldehyde. An example of this. . . may be activated as described above. The activated amine groups can be used, in turn, to couple to a functionalized **hydrophilic** polymer, such as, for example, α-amino-ω-hydroxy-PEG in which the ω-hydroxy group has been protected with a carbonate group. After the. . .

DETD . . . of a dialdehyde, for example, glutaraldehyde as described above, to form a Schiff's base. After linking the DPPE to the **hydrophilic** polymer and the targeting ligand, the vesicles may be formulated utilizing the procedures described herein.

DETD . . . procedures, the polymer or terminus of the lipid, for example, phosphatidylglycerol or phosphatidylethanolamine, is preferably activated and coupled to the **hydrophilic** polymeric linker, the

terminus of which has been blocked in a suitable manner. As an example of this strategy, α-amino-ω-carboxy-PEG4000. . .

DETD The free end of the **hydrophilic** spacer, such as polyethylene glycol ethylamine, which contains a reactive group, such as an amine or hydroxyl group, may be. . . will be evaporated to dryness under argon. Excess unreacted SMPB and major by products will be removed by preparative thin **layer** chromatography (TLC, silica gel developed with 50% acetone in chloroform). The upper portion of the lipid band can be extracted. . .

DETD The targeted compounds of the present invention are incorporated in compositions which may be used to form targeted **emulsions** and/or targeted vesicles, including, for example, targeted **emulsions**, targeted **micelles**, targeted liposomes, targeted albumin coated microspheres, targeted polymer coated microspheres, targeted cochleates and the like. The targeting ligand which is. . .

DETD . . . network, and the like. Non-covalent bonds are preferably selected from the group consisting of ionic interaction, dipole--dipole interaction, hydrogen bonds, **hydrophilic** interactions, van der Waal's forces, and any combinations thereof. Non-covalent interactions may be employed to bind the targeting ligand to. . .

DETD wherein L is a lipid, protein, polymer, carbohydrate, surfactant, photoactive agent or the like; P is a **hydrophilic** polymer; and T is a targeting ligand.

DETD In the above compounds, P is a **hydrophilic** polymer. Preferably, P is a **hydrophilic** polymer selected from the group consisting of polyalkyleneoxides, polyvinyl alcohol, polyvinylpyrrolidones, polyacrylamides, polymethacrylamides, polyphosphazenes, phosphazene, poly(hydroxyalkylcarboxylic acids) and polyoxazolidines. More. . .

DETD . . . --; each n is, independently, 0 or 1; Y is hydrogen or a pharmaceutically acceptable counter ion; Z is a **hydrophilic** polymer; Q is a targeting ligand or a precursor to a targeting ligand; each R.sub.1 is independently an alkyl group. . .

DETD In the above formula, Z is a **hydrophilic** polymer. Preferably, Z is selected from the group consisting of polyalkyleneoxides, polyvinyl alcohol, polyvinylpyrrolidones, polyacrylamides, polymethacrylamides, polyphosphazenes, poly(hydroxyalkyl-carboxylic acids) and. . . polyethylene glycol and polypropylene glycol, with polyethylene glycol being still more preferred. In certain other preferred embodiments, Z is a **hydrophilic** polymer other than polyalkylene-oxides, including polyethylene glycol and polypropylene glycol. The molecular weight of Z may vary, depending, for example,. . .

DETD A wide variety of methods are available for the preparation of the stabilizing materials, including vesicles, such as **micelles** and/or liposomes. Included among these methods are, for example, shaking, drying, gas-installation and spray drying. Suitable methods for preparing vesicle. . .

DETD **Micelles** may be prepared using any one of a variety of conventional **micellar** preparatory methods which will be apparent to one skilled in the art. These methods typically involve suspension of the stabilizing. . . discussed, for example, in Canfield et al, Methods in Enzymology, 189:418 (1990); El-Gorab et al, Biochem. Biophys. Acta, 306:58 (1973); **Colloidal** Surfaciant, Shinoda, K., Nakagana, Tamamushi and Isejura, Academic Press, NY (1963) (especially "The Formation of **Micelles**," Shinoda, Chapter 1, pp. 1-88); Catalysis in **Micellar** and Macromolecular Systems, Fendler and Fendler, Academic Press, NY (1975). The disclosures of each of the foregoing publications are hereby. . .

DETD In liposomes, the lipid compound(s) may be in the form of a

monolayer or **bilayer**, and the **monolayer** or **bilayer** lipids may be used to form one or more **monolayers** or **bilayers**. In the case of more than one **monolayer** or **bilayer**, the **monolayers** or **bilayers** are generally concentric. Thus, lipids may be used to form **unilamellar** liposomes (comprised of one **monolayer** or **bilayer**), **oligolamellar** liposomes (comprised of two or three **monolayers** or **bilayers**) or **multilamellar** liposomes (comprised of more than three **monolayers** or **bilayers**).

DETD . . . solvent dialysis, French press, extrusion (with or without freeze-thaw), reverse phase evaporation, simple freeze-thaw, sonication, chelate dialysis, homogenization, solvent infusion, **microemulsification**, spontaneous formation, solvent vaporization, solvent dialysis, French pressure cell technique, controlled detergent dialysis, and others, each involving the preparation of. . . Praeparate GMBH & Co., Seefeld, Oberay Germany), a Silamat Plus (Vivadent, Lechtenstein), or a Vibros (Quayle Dental, Sussex, England). Conventional **microemulsification** equipment, such as a Microfluidizer.TM. (Microfluidics, Woburn, Mass.) may also be used.

DETD . . . to liquid crystalline phase transition temperature of the lipids. This phase transition temperature is the temperature at which a lipid **bilayer** will convert from a gel state to a liquid crystalline state. See, for example, Chapman et al, J. Biol. Chem.,. . . crystalline state phase transition temperatures tend to have enhanced impermeability at any given temperature. See Marsh, CRC Handbook of Lipid **Bilayers** (CRC Press, Boca Raton, Fla. 1990), at p. 139 (the disclosure of which is hereby incorporated by reference herein in. . .

DETD . . . No. 08/307,305, filed Sep. 16, 1994, the disclosures of each of which are incorporated herein by reference in their entirety. **Emulsion** processes may also be employed in the preparation of compositions in accordance with the present invention. Such **emulsification** processes are described, for example, in Quay, U.S. Pat. Nos. 5,558,094, 5,558,853, 5,558,854, and 5,573,751, the disclosures of each of. . .

DETD **Microemulsification** is a common method of preparing an **emulsion** of a foam precursor. Temperature increases and/or lowered pressures will cause foaming as gas bubbles form in the liquid. As. . .

DETD The size of gas filled vesicles can be adjusted, if desired, by a variety of procedures, including, for example, **microemulsification**, vortexing, extrusion, filtration, sonication, homogenization, repeated freezing and thawing cycles, extrusion under pressure through pores of defined size, and similar. . .

DETD . . . gas is incorporated, for example, into a vesicle. For gaseous precursors having low temperature boiling points, liquid precursors may be **emulsified** using a microfluidizer device chilled to a low temperature. The boiling points may also be depressed using solvents in liquid. . .

DETD . . . a temperature below the liquid-gaseous phase transition temperature of the respective gaseous precursor. As the temperature is increased, and an **emulsion** is formed between the gaseous precursor and liquid solution, the gaseous precursor undergoes transition from the liquid to the gaseous. . .

DETD As a further embodiment of this invention, by pre-forming the gaseous precursor in the liquid state into an aqueous **emulsion**, the maximum size of the vesicle may be estimated by using the ideal gas law,

once the transition to the. . . due to diffusion into the liquid, which is generally aqueous in nature. Hence, from a known liquid volume in the **emulsion**, one would be able to predict an upper limit to the size of the gas filled vesicle.

DETD . . . to form a vesicle with an upper limit of 10 μm. Finally, using equation (C), a mixture, for example, an **emulsion** containing droplets with a radius of 0.0272 μm or a corresponding diameter of 0.0544 μm, is formed to make a. . .

DETD An **emulsion** of this particular size could be easily achieved by the use of an appropriately sized filter. In addition, as seen. . .

DETD . . . be performed during in vivo administration of the vesicles such that a filter of about 0.22 μm is employed; (b) **microemulsification** whereby an aqueous mixture of gaseous precursor is **emulsified** by agitation and heated to form, for example, vesicles prior to administration to a patient; (c) heating a gaseous precursor. . .

DETD . . . as about 30 minutes, preferably within about 20 minutes, and more preferably within about 10 minutes. The shaking may involve **microemulsifying**, microfluidizing, swirling (such as by vortexing), side-to-side, or up and down motion. In the case of the addition of gaseous. . .

DETD . . . prepared as described above in which the compositions also comprise photoactive agents, bioactive agents and/or targeting ligands. Thus, for example, **micelles** can be prepared in the presence of a photoactive agent, bioactive agent and/or targeting ligand. In connection with lipid compositions. . .

DETD . . . temperature below the liquid-gaseous phase transition temperature of the respective gaseous precursor. As the temperature is then exceeded, and an **emulsion** is formed between the gaseous precursor and liquid solution, the gaseous precursor undergoes transition from the liquid to the gaseous. . . entrapped fluorobutane gas results. As an additional example, the gaseous precursor fluorobutane, can be suspended in an aqueous suspension containing **emulsifying** and stabilizing agents such as glycerol or propylene glycol and vortexed on a commercial vortexer. Vortexing is commenced at a. . . transition temperature from the liquid to gaseous state. In so doing, the precursor converts to the gaseous state during the **microemulsification** process. In the presence of the appropriate stabilizing agents, surprisingly stable gas filled vesicles and photoactive agents, bioactive agents and/or. . .

DETD . . . that a solvent, a surfactant, and a photoactive agent, a targeting ligand and/or bioactive agent are combined to form an **emulsion** in the form of a random aggregate. In the case of spray drying, the **emulsion**, or **colloidal** suspension, is placed into association with a blowing agent such as methylene chloride, for example. Each of the ingredients of. . . as a phospholipid or a fluorosurfactant, within aqueous or organic media, the former being preferred. Additionally, some nonpolar photoactive agent **emulsions** may contain an oil to effect solubilization. As the suspension or **emulsion** is then spray dried, the photoactive agent and/or bioactive agent dries and the blowing agent and solvent are removed tending. . .

DETD . . . lyophilization. A bulk quantity of the composition of the present invention may be prepared with a ball mill or a **colloid** mill device. The appropriate sized crystalline particles are prepared, generally under 10 μm, preferably under 5 μm and still more. . .

DETD . . . a patient's lungs. For pulmonary applications, dried or lyophilized powdered compositions may be administered via inhaler. Aqueous suspensions of liposomes, **micelles** or other vesicles, preferably gas/gaseous precursor filled, may be administered via

nebulization. The compositions of the present invention are lighter. . .

DETD . . . of the vesicles can be adjusted, if desired, by procedures known to one skilled in the art, such as shaking, **microemulsification**, vortexing, filtration, repeated freezing and thawing cycles, extrusion, extrusion under pressure through pores of a defined size, sonication, homogenization, the. . .

DETD Perfluoropropane encapsulated lipid **bilayers** were formed with a lipid formulation comprising 5 mg/ml of a mixture comprising 82 mole % dipalmitoylphosphatidylcholine, 10 mole %. . . Lipids, Alabaster, Ala.) in a vehicle comprising 8:1:1 of v:v:v normal saline:propylene glycol:glycerol, yielding a foam and a lower vehicle **layer** that was predominantly devoid of any particulate. To this mixture was added 1 mg/ml of dipalmitoylphosphatidylethanol-amine derivatized with lissamine rhodamine. . .

DETD . . . Capmix for two minutes at 4,500 rpm. Variations of the vehicle yielded varying degrees of clarity to the lower vehicle **layer.** Prior to filtration, the gas-filled microspheres were sized on a Particle Sizing SYstems Model 770 optical sizer (Particle Sizing Systems,. . .

DETD . . . minutes at 50° C. then transferred into a container with 200 mls normal saline plus 1% w/v Pluronic F-65 and **emulsified** with a Microfluidizer (10+) at 16,000 psi while the temperature was maintained at 50° C. The material was then subdivided. . .

DETD . . . poured into ice water and neutralized with 10% HCl to a pH of about 3 or less. The lower organic **layer** was removed using a separatory funnel and washed three times with water. The organic **layer** was collected and dried (NaSO.sub.4). Filtration and concentration in vacuo yielded 0.34 g of a white solid of 3-ω-carboxy-polyethyleneglycol-imino-succinat-1,2-dipalmitoyl-sn-glycerol (DPGS-ω-carboxy-PEG).

DETD . . . poured into ice water and neutralized with 10% HCl to a pH of about 3 or less. The lower organic **layer** was removed using a separatory funnel and washed three times with water. The organic **layer** was collected and dried (NaSO.sub.4). Filtration and concentration in vacuo yielded 0.34 g of a white solid of 3-ω-carboxypolyethyleneglycol-imino-succinat-1,2-dipalmitoyl-sn-glycerol (DPGS-6-carboxy-PEG).

IC [7]
ICM: **A61K049-00**
ICS: A61K049-22

IT 106-60-5, δ-Aminolevulinic acid 302-79-4, Retinoic acid 302-79-4D, Retinoic acid, derivs. 479-61-8 553-12-8, Protoporphyrin IX 574-93-6D, Phthalocyanine, derivs. 603-34-9D, Triphenylamine, derivs. 643-79-8, o-Phthaldialdehyde 917-23-7D, Tetraphenylporphine, sulfonated derivs. 1075-06-5, Phenylglyoxal monohydrate 1210-12-4, 9-Anthronitrile 2321-07-5D, Fluorescein, derivs. 3599-32-4, Indocyanine green 5143-18-0 7149-49-7, Naphthalene-2,3-dicarboxaldehyde 12713-07-4D, Verdin, derivs. 12778-00-6, Mesochlorin 13558-31-1D, derivs. 14325-05-4, Tin protoporphyrin 14459-29-1, Hematoporphyrin 19660-77-6, Chlorin e6 19660-77-6D, Chlorin e6, mono-L-aspartyl derivative 23627-89-6D, Naphthalocyanine, derivs. 25440-13-5 26038-83-5, 4-Heptadecyl-7-hydroxycoumarin 41085-99-8 41387-42-2 60415-70-5D, 21H,23H-Porphin-5(22H)-one, derivs. 61494-52-8, 1-Pyrenesulfonyl chloride 62796-29-6, Lissamine rhodamine B sulfonyl chloride 62888-19-1, Bonellin 65603-18-1 65603-19-2, Octadecyl rhodamine B chloride 68335-15-9, Photofrin 72467-67-5 72535-39-8 73024-99-4, 12-(9-Anthroyloxy)oleic acid 75168-11-5 76081-97-5, Cholesteryl 1-pyrenebutyrate 78949-95-8 88235-25-0 88478-07-3 95864-17-8 96886-70-3 97850-83-4, Cholesteryl

1-pyrenedecanoate 99128-91-3, Octaethylpurpurin 100572-96-1D,
Porphycene, compds. 105344-74-9 113471-15-1 114041-00-8
114494-17-6 114586-25-3 115645-42-6 123738-53-4 123940-54-5,
Hypocrellin B 128146-77-0 134020-79-4D, Sapphyrin, derivs.
135615-37-1D, Rubyrin, derivs. 138026-68-3 147662-88-2,
2-Dodecylresorufin **151736-99-1** 151892-94-3 186833-02-3
216434-81-0 217187-10-5 227936-56-3D 2λ4-1,2,5-
Oxatellurazole, d
(as photoactive trast agents and methods for
their use in ul ging)

See structure p. 35

=> FIL STNGUIDE

FILE 'STNGUIDE' ENTERED 004
USE IS SUBJECT TO THE T REEMENT
COPYRIGHT (C) 2004 AMER APAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 21, 2004 (20040521/UP).

=>

=> fil zcaplus

FILE 'ZCAPLUS' ENTERED AT 12:49:02 ON 27 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 May 2004 VOL 140 ISS 22
FILE LAST UPDATED: 26 May 2004 (20040526/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 12:49:06 ON 27 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 27 May 2004 VOL 140 ISS 22
FILE LAST UPDATED: 26 May 2004 (20040526/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> fil biosis

FILE 'BIOSIS' ENTERED AT 12:49:09 ON 27 MAY 2004

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 May 2004 (20040526/ED)

```
FILE RELOADED: 19 October 2003.

=> FIL STNGUIDE

FILE 'STNGUIDE' ENTERED AT 12:49:14 ON 27 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: May 21, 2004 (20040521/UP).

=> d que l124
L121        134 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LU/AU OR "LU D"/AU OR "LU D
                R"/AU OR "LU D ROBERT"/AU OR ("LU DONGHAO"/AU OR "LU DONGHAO
                R"/AU OR "LU DONGHAO ROBERT"/AU)
L122         10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("SHAWER M"/AU OR "SHAWER M
                B"/AU OR "SHAWER M F"/AU OR "SHAWER MOHANNAD"/AU)
L124          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L121 AND L122


=> d que l130
L83         168 SEA FILE=BIOSIS ABB=ON  PLU=ON  ?CHOLEST? (L) (?BORO? OR
                ?BORIC? OR ?BORAN? OR ?BORAX?)
L84      633075 SEA FILE=BIOSIS ABB=ON  PLU=ON  (?COLLOID? OR ?EMULS? OR
                ?LAYER? OR ?CORE? OR ?AMPHIPATH? OR ?HYDROPHOB? OR ?HYDROPHIL?
                OR ?LAMEL? OR ?MICELL?)
L86          28 SEA FILE=BIOSIS ABB=ON  PLU=ON  L84 AND L83
L87          10 SEA FILE=BIOSIS ABB=ON  PLU=ON  L86 AND (TETRAPHENYLBORON OR
                BORON NEUTRON-CAPTURE OR BORON NEUTRON CAPTURE OR MURINE
                TUMORS OR XENOGRAFTS OR BNCT OR VLDL OR CHOLESTERYL CARBORANE)/
                TI
L88          31 SEA FILE=BIOSIS ABB=ON  PLU=ON  L83 AND (?DRUG? OR ?RADIOTHER?
                OR ?IMAG? OR ?PHARMACEUT?)
L89          25 SEA FILE=BIOSIS ABB=ON  PLU=ON  L88 NOT L86
L90           6 SEA FILE=BIOSIS ABB=ON  PLU=ON  L89 AND (BRATTLEBORO OR DRUG
                DELIVERY OR BORON NEUTRON CAPTURE)/TI
L91           5 SEA FILE=BIOSIS ABB=ON  PLU=ON  L90 NOT CORTICAL/TI
L93          15 SEA FILE=BIOSIS ABB=ON  PLU=ON  L87 OR L91
L120         13 SEA FILE=BIOSIS ABB=ON  PLU=ON  L93 NOT (BRATTLEBORO OR
                TETRAPHENYLBORON)/TI
L127        333 SEA FILE=BIOSIS ABB=ON  PLU=ON  LU/AU OR "LU D"/AU OR ("LU D
                R"/AU OR "LU D ROBERT"/AU) OR "LU DONGHAO ROBERT"/AU
L128         38 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("SHAWER M"/AU OR "SHAWER M
                B"/AU OR "SHAWER M F"/AU OR "SHAWER MOHANNAD"/AU) OR ("SHAWER
                M"/AU OR "SHAWER M B"/AU OR "SHAWER M F"/AU OR "SHAWER
                MOHANNAD"/AU)
L129          2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L127 AND L128
L130          1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L129 NOT L120


=> dup rem l124 l130

FILE 'HCAPLUS' ENTERED AT 12:49:41 ON 27 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 12:49:41 ON 27 MAY 2004
```

PROCESSING COMPLETED FOR L124
PROCESSING COMPLETED FOR L130
L132 3 DUP REM L124 L130 (1 DUPLICATE REMOVED)
ANSWERS '1-3' FROM FILE HCAPLUS

=> d ibib abs l132 1-3

L132 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:316317 HCAPLUS
DOCUMENT NUMBER: 139:369467
TITLE: In vitro gene transfection in human glioma cells using a novel and less cytotoxic artificial lipoprotein delivery system
AUTHOR(S): Pan, Guangliang; **Shawer, Mohannad**; Oie, Svein; **Lu, D. Robert**
CORPORATE SOURCE: College of Pharmacy, Department of Pharmaceutical and Biomedical Sciences, University of Georgia, Athens, GA, 30602, USA
SOURCE: Pharmaceutical Research (2003), 20(5), 738-744
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To develop and evaluate a novel artificial lipoprotein delivery system for in vitro gene transfection in human glioma cells. Nanoemulsion was formulated with similar lipid compns. present in natural lipoproteins. The oil phase of nanoemulsion was composed of triolein (70%), egg phosphatidylcholine (22.7%), lysophosphatidylcholine (2.3%), cholesterol oleate (3.0%), and cholesterol (2.0%). To replace the surface protein as in natural lipoprotein, poly-L-lysine was modified to add palmitoyl chains at a basic condition and was incorporated onto the nanoemulsion particles through hydrophobic interaction. A model plasmid DNA, pSV-β-Gal containing a reporter gene for β-galactosidase was carried by the nanoemulsion/poly-L-lysine particles. The charge variation of so-formed complex was examined by agarose gel electrophoresis and zeta potential measurement. In vitro transfection was conducted on human SF-767 glioma cell line using this new system. After standard X-Gal staining, transfected cells were observed under light microscope. The effect of chloroquine on the transfection was examined and, finally, the cytotoxicity of this new system was evaluated in comparison with com. Lipofectamine gene transfection system. The plasmid DNA was effectively carried by this artificial lipoprotein delivery system and the reporter gene was expressed in the glioma cells. Transfection efficiency was significantly increased by the treatment of chloroquine, indicating that endocytosis possibly was the major cellular uptake pathway. Compared to Lipofectamine system, this new delivery system demonstrated similar transfection efficiency but a much lower cytotoxicity. In the experiment, the cell viability showed up to 75% using this system compared to only 24% using Lipofectamine system. A new artificial lipoprotein delivery system was developed for in vitro gene transfection in tumor cells. The new system showed similar transfection efficiency but a much lower cytotoxicity compared with com. Lipofectamine system.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:431808 HCAPLUS
DOCUMENT NUMBER: 138:192980
TITLE: VLDL-resembling phospholipid-submicron emulsion for

cholesterol-based drug targeting
AUTHOR(S): **Shawer, Mohannad**; Greenspan, Phillip; Oie, Svein; **Lu, D. Robert**
CORPORATE SOURCE: Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, University of Georgia, Athens, GA, 30602, USA
SOURCE: Journal of Pharmaceutical Sciences (2002), 91(6), 1405-1413
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of the current study was to develop and evaluate VLDL-resembling phospholipid-submicron emulsion (PSME) as a carrier system for new cholesterol-based compds. for targeted delivery to cancer cells. BCH, a boronated cholesterol compound, was originally developed in our laboratory to mimic the cholesterol esters present in the LDL and to follow a similar pathway of cholesterol transport into the rapidly dividing cancer cells. The VLDL-resembling system was then designed to solubilize BCH, facilitate the interaction with LDL, and thus assist the BCH delivery to cancer cells. BCH-containing PSME was prepared by sonication. Chemical compns. and particle sizes of different PSME fractions were determined The lipid structure of PSME and location of BCH in the formulation were assessed based on exptl. results. D. gradient ultracentrifugation fractionated the emulsion into three particle-size populations with structures and compns. resembling native VLDL. In vitro interaction between PSME and LDL was evident by agarose electrophoresis, as both formed a single band with an intermediate mobility. The transfer of BCH from PSME to LDL was also observed in the presence of other serum components including serum proteins. Cell culture data showed sufficient uptake of BCH in rat 9L glioma cells (> 50 μg boron/g cells). In conclusion, this system has the capability to incorporate the cholesterol-based compound, interact with native LDL, and assist the delivery of this compound into cancer cells in vitro.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L132 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:672328 HCAPLUS
DOCUMENT NUMBER: 134:212541
TITLE: A new approach for targeted boron drug delivery to brain tumor
AUTHOR(S): **Lu, D. R.**; Ji, B.; Peacock, G.; **Shawer, M.**
CORPORATE SOURCE: University of Georgia, Athens, GA, 30602, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (2000), 27th, 808-809
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cholesteryl 1,12-dicarba-closo-dodecaborane-1-carboxylate was prepd and had good cellular uptake efficiency. The approach may be useful for targeted boron drug delivery to brain tumor cells.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL STNGUIDE

```
=> log h
```